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TO: Ralph J Gitomer **Location: 3e65 / 3e71** **Wednesday, July 07, 2004** **Art Unit: 1651** **Phone: 272-0916** **Serial Number: 10 / 663449**	**From: Jan Delaval** **Location: Biotech-Chem Library** **Rem 1A51** **Phone: 272-2504** **jan.delaval@uspto.gov**

Search Notes

JAN 125480

Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: R Gitomer Examiner # : _____ Date: 6/23/04

Art Unit: 1651 Phone Number 30_____ Serial Number: 10/663,449

Mail Box and Bldg/Room Location: 3671 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

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Title of Invention: _____

Inventors (please provide full names): _____

_____

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

JAN

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JUN 23 2004
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Searcher Phone #: 72500	AA Sequence (#)		Dialog	
Searcher Location:	Structure (#)		Questel/Orbit	
Date Searcher Picked Up: 7/7	Bibliographic	✓	Dr.Link	
Date Completed: 7/7	Litigation		Lexis/Nexis	
Searcher Prep & Review Time:	Fulltext		Sequence Systems	
Clerical Prep Time: 20	Patent Family		WWW/Internet	
Online Time: 70	Other		Other (specify)	

PTO-1590 (8-01)

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=> fil wpix
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MOST RECENT DERWENT UPDATE:     200442        <200442/DW>
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    NEW FORMAT GERMAN PATENT APPLICATION AND PUBLICATION
    NUMBERS. SEE ALSO:
    http://www.stn-international.de/archive/stnews/news0104.pdf <<<

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L62  ANSWER 1 OF 41  WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN   2004-203810 [19]    WPIX
DNN  N2004-161906        DNC C2004-080473
TI   Determination of concentration of free thrombin in e.g.
     blood, involves measuring physical property of the product as
     function of time, and determining time derivative of
     the concentration of alpha-macroglobulin-thrombin complex.
DC   B04 D16 S03
IN   HANSSON, G
PA   (ASTR) ASTRAZENECA AB
CYC  105
PI   WO 2004016807   A1 20040226 (200419)* EN   32    C12Q001-56     <--
        RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS
            LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH
            PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC
            VN YU ZA ZM ZW
ADT  WO 2004016807 A1 WO 2003-SE1273 20030813
PRAI SE 2002-2454         20020816
IC   ICM  C12Q001-56
     ICS  G01N033-49; G01N033-86
ICA  A61P007-02
AB   WO2004016807 A UPAB: 20040318
     NOVELTY - A concentration of free thrombin in sample is
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determined as a function of **time** by measuring a physical property of the product as a function of **time**, computing a **time** derivative of the physical property to determine a **rate** of reaction from the substrate to product, and determining the concentration of free **thrombin**, from a **time** derivative of the concentration of alpha-macroglobulin-**thrombin** complex (alpha 2MT).

DETAILED DESCRIPTION - Determination of concentration of free **thrombin** in a sample as a function of **time** comprises providing a substrate that reacts with **thrombin** to form a product, measuring a physical property of the product as a function of **time**, computing a **time** derivative of the physical property to determine a **rate** of reaction from the substrate to product, deterring the concentration of alpha 2MT as a function of **time**, and determining the concentration of free **thrombin** , from a **time** derivative of the concentration of alpha 2MT.

INDEPENDENT CLAIMS are also included for:

(1) an apparatus for determining a concentration of free **thrombin** in a sample as a function of **time** comprising physical property measuring element, **time** derivative computing device, and free **thrombin** determining device. used in the invention; and

(2) assessing the effectiveness of putative **anticoagulant**, comprising providing a sample containing a **thrombin** precursor, determining the concentration of free **thrombin** in the sample as a function of **time** using the **method**, and assessing whether the **rate** of free **thrombin** formation determined is indicative of **anticoagulant** activity.

USE - For determining a concentration of free **thrombin** in a sample, e.g. **blood** and/or **blood plasmas.**

ADVANTAGE - The inventive **method** provides more accurate determination of free **thrombin** concentration in the sample.

DESCRIPTION OF DRAWING(S) - The drawing shows a schematic diagram of the process for **thrombin** induced conversion of a substrate to product yielding a measurable change in optical properties of the product.

Dwg.1/3

FS CPI EPI

FA AB; GI

MC CPI: **B04-B04D4; B04-B04D5; B04-H19;** B11-C08E; B12-K04; D05-H08; **D05-H09;** D05-H13

EPI: **S03-E14H; S03-E14H1**

TECH UPTX: 20040318

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred **Method** : The **method** further comprises iteratively varying values for parameter k, expressing the relationship between the **rate** of change of concentration of alpha2MT and a concentration of free **thrombin**, or parameter, kcat2, expressing a **rate** of turnover of substrate by alpha2MT, to reduce an optimization value. The determining of the concentration of alpha2MT includes assuming the initial condition of t = 0 of (alpha2MT) = 0. The **method** also includes predetermining a **rate** of turnover of substrate from **thrombin**, kcat2, and predetermining the Michaelis constant, k-M for the substrate, **thrombin**, and alpha2MT. Preferred Parameters: The optimization value incorporates a value, RMSE, expressing a difference between a measured value of the physical property of the product and a calculated combined value related to the concentrations of free **thrombin** and alpha2MT. The optimization value further comprises a factor related to the calculated average free **thrombin** concentration during a preceding period of **time.** The value RMSE comprises the mathematical equation (I). (Structure (I), page 20)

P = concentration of product at **time**;

a1 = reaction **rate** from substrate to product by **thrombin**;

kcat1 = **rate** of turnover of substrate by **thrombin**;
and
kcat2 = **rate** of turnover of substrate by alpha-MT.

L62 ANSWER 2 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **2003-723490** [69] WPIX
DNN **N2003-578477** DNC **C2003-199290**
TI Test strip qualification **method** for measuring **prothrombin time** with whole **blood** by obtaining **prothrombin time** results, and **comparing** result from two control areas to two control qualification criteria.
DC B04 S03
IN PATEL, H; PATEL, H I
PA (LIFE-N) LIFESCAN INC; (PATE-I) PATEL H
CYC 38
PI EP 1345030 A1 20030917 (200369)* EN 11 G01N033-49 <--
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
NO 2003000903 A 20030915 (200369) G01N033-52 <--
CA 2421467 A1 20030914 (200372) EN G01N033-86 <--
JP 2003294759 A 20031015 (200376) 9 G01N033-86 <--
CN 1445550 A 20031001 (200382) G01N033-86 <--
US 2003175978 A1 20030918 (200382) G01N031-00
KR 2003074409 A 20030919 (200410) G01N033-52 <--
US 6673617 B2 20040106 (200411) G01N031-00
AU 2003200892 A1 20031002 (200428) G01N033-86 <--
US 2004096980 A1 20040520 (200434) G01N021-00
ADT EP 1345030 A1 EP 2003-251534 20030313; NO 2003000903 A NO 2003-903 20030226; CA 2421467 A1 CA 2003-2421467 20030310; JP 2003294759 A JP 2003-68305 20030313; CN 1445550 A CN 2003-120515 20030313; US 2003175978 A1 US 2002-100531 20020314; KR 2003074409 A KR 2003-15615 20030313; US 6673617 B2 US 2002-100531 20020314; AU 2003200892 A1 AU 2003-200892 20030228; US 2004096980 A1 Cont of US 2002-100531 20020314, US 2003-712679 20031112
FDT US 2004096980 A1 Cont of US 6673617
PRAI US 2002-100531 20020314; US 2003-712679 20031112
IC ICM G01N021-00; G01N031-00; **G01N033-52**; **G01N033-86**
ICS **A61B005-000**; **C12Q001-56**; G06F015-04
ICA **G01N033-49**
AB EP 1345030 A UPAB: 20031027
NOVELTY - Test strip qualification **method** comprises:
(1) providing a test strip (2);
(2) obtaining **prothrombin time** (PT) results for each reaction area;
(3) **comparing** result from first and second control areas to first and second control qualification criteria, respectively; and
(4) outputting message to user indicating test strip reliability.
DETAILED DESCRIPTION - Test strip qualification **method** comprises:
(1) providing a test strip;
(2) obtaining **prothrombin time** (PT) results for each reaction area;
(3) **comparing** result from the first and second control areas to first and second control qualification criteria, respectively; and
(4) outputting a message to user indicating test strip reliability.
The test strip comprises assay reaction area, and two control reaction areas. The first control qualification criteria comprise upper and lower limits. The first control upper limit is at least partially dependent upon assay reaction area PT result.
INDEPENDENT CLAIMS are also included for:
(1) system programmed to operate according to the **method**; and

(2) computer-readable medium using a program to direct system to perform the **method.**

USE - The **method** is useful in measuring **prothrombin time** (PT) (claimed) with whole **blood.**

ADVANTAGE - The **method** provides test strip that gives highly accurate and reliable results.

DESCRIPTION OF DRAWING(S) - The figure shows a top view of the test strip.

Test strip 2

Measurement areas 4, 6, 8

Introduction port 10

Bladder 12

Channel 14

Junction 16

Bypass channel 18

Dwg.1a/5

FS CPI EPI

FA AB; GI; DCN

MC CPI: **B04-B04D5; B04-H19;** B11-C08; B12-K04

EPI: **S03-E14H; S03-E14H1**

TECH UPTX: 20031027

TECHNOLOGY FOCUS - MECHANICAL ENGINEERING - Preferred Components: The upper limit is dependent upon assay reaction area PT results at most2 international **normalized ratio** (INR). The upper limit comprises linear function dependent upon assay reaction area PT results. The upper limit also comprises a value independent of assay reaction area PT result for reaction area PT result at least2 INR. The lower limit comprises value independent of assay reaction PT result. The PT results obtained for each reaction area are INR values. The second control qualification criteria comprise upper and lower limits. The lower limit has two sections dependent upon assay reaction area PT results. The second control drops-off from the first section.

L62 ANSWER 3 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN **2002-489927** [52] WPIX

DNN **N2002-387327** DNC **C2002-139068**

TI Novel reagent useful for assessment of **hemostatic** potential of **blood** or **plasma** sample, comprises a **coagulation activator.**

DC B04 D16 P31

IN **BAGLIN, T**; DOOBAY, H; **FISCHER, T J**; LUDDINGTON, R; **TEJIDOR, L**

PA (**ALKU**) **AKZO NOBEL NV**; (BIOM-N) BIO MERIEUX INC; (**INMR**) **BIOMERIEUX INC**

CYC 98

PI WO 2002034109 A2 20020502 (200252)* EN 44 A61B000-00 <--

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2002015382 A 20020506 (200257) A61B000-00 <--

EP 1337858 A2 20030827 (200357) EN G01N033-86 <--

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

US 6645768 B1 20031111 (200382) G01N033-86 <--

BR 2001014942 A 20031223 (200406) G01N033-86 <--

JP 2004512511 W 20040422 (200428) 70 G01N033-48 <--

ADT WO 2002034109 A2 WO 2001-US32563 20011018; AU 2002015382 A AU 2002-15382 20011018; EP 1337858 A2 EP 2001-983998 20011018, WO 2001-US32563 20011018; US 6645768 B1 US 2000-698589 20001027; BR 2001014942 A BR 2001-14942 20011018, WO 2001-US32563 20011018; JP 2004512511 W WO 2001-US32563

20011018, JP 2002-537169 20011018
FDT AU 2002015382 A Based on WO 2002034109; EP 1337858 A2 Based on WO 2002034109; BR 2001014942 A Based on WO 2002034109; JP 2004512511 W Based on WO 2002034109
PRAI US 2000-698589 20001027
IC ICM **A61B000-00**; **G01N033-48**; **G01N033-86**
ICS C07K004-00; **C12Q001-56**; G01N035-02
AB WO 200234109 A UPAB: 20020815
NOVELTY - A reagent (I) comprising a **coagulation activator** at a concentration of 11 picomolar or less, for assessment of the **hemostatic** potential of a **blood** or **plasma** sample, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a kit for assessing the **hemostatic** potential of a test sample comprising a **coagulation activator** at a concentration of 11 picomolar or less, or the **activator** and instructions for diluting the **activator**, **vesicles**, a metal divalent **cation** or a metal salt capable of dissociating into a metal divalent **cation**, instructions for adding the **activator**, metal **cation** or metal salt and **vesicles** to a test sample, and instructions for assessing the **hemostatic** potential of the test sample.

USE - The reagent and the kit are useful for indicating a sample to be **hypocoagulable**, **normal** or **hypercoagulable**, depending upon the condition of the patient from which the sample was taken, for indicating a patient to have **thrombotic** tendency, hemorraghic tendency, or stasis, and also for assessing **hemostatic** potential of a **blood** or **plasma** sample (claimed). (I) is useful in the drug discovery and drug development processes by modifying the components or concentrations of the reagent. (I) is useful to determine the amount of **plasma** to be modified in order to restore **coagulability** to **normal**.

ADVANTAGE - The reagent allows for globally assessing both the **hypercoagulable** potential and **hypocoagulable** potential of a patient in a single assay, which is accurate, sensitive and easy. The test is simple and can be automated on **standard** laboratory **coagulometers**. The test is based on the **rate** of **fibrin polymerization** which allows detection of perturbances in the propagation, amplification and **polymerization pathways**, whereas in the traditional **prothrombin time** test, these parts of the **coagulation pathway** are overshadowed by the excessive amounts of Factor IIa produced by the **initiation** phase.

Dwg.0/10
FS CPI GMPI
FA AB; DCN
MC CPI: **B04-B04D4**; **B04-B04D5**; **B04-H19**; B04-N02; B05-A01B; B05-A03A; B05-B01P; B05-C07; B11-C08E; B12-K04A; **D05-H09**
TECH UPTX: 20020815
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Reagent: (I) further comprises **vesicles** or liposomes. The **vesicles** comprise **platelets**, cellular debris, **phospholipid vesicles** (prepared by dilution, sonication, dialysis or extrusion), or **platelet** microparticles. The **coagulation activator** comprises **tissue factor** which is a recombinant or purified, truncated **tissue factor**, or cells expressing **tissue factor** on their surface. The **tissue factor** comprises a metal **cation**, especially a divalent metal **cation** such as magnesium, calcium or manganese or metal salt (5-50, preferably 15-35 mM), preferably a halide of magnesium, calcium or manganese, which dissociates into a metal **cation**. The **tissue factor** is at a

concentration of 11, 8 or 6 picomolars, preferably 3 picomolars or less. The **vesicles** comprise **phospholipids** (at a concentration of 10-300 micromolar, preferably 50-200 micromolar) which comprise one or more of phosphatidylcholine, phosphatidylethanolamine or phosphatidylserine at a **ratio** of 0-10, preferably 10 %, by mole phosphatidylserine, 5-30, preferably 20 %, by mole phosphatidylethanolamine and the remainder, preferably 70 %, by mole phosphatidylcholine. The **coagulation activator** comprises **tissue factor**-rich mammalian tissue extracts, **tissue factor** purified from mammalian tissue or **thromboplastin.** The **coagulation activator** is capable of detecting defects in the **initiation** phase. (I) further comprises an **activator** of an **anticoagulant pathway**, preferably an **activator** of **protein C** which is a purified human or non-human mammalian **thrombomodulin**, soluble or membrane associated **thrombomodulin**, native **thrombomodulin** or **thrombomodulin** reconstituted with **phospholipids**, partially or fully glycosylated **thrombomodulin**, and fully deglycosylated **thrombomodulin.** The **protein C activator** (**thrombomodulin**) is at a concentration of 30 nanomolar or less, preferably 5-20 nanomolar. The **thrombomodulin** comprises heparin or heparin-like molecules and is relipidated with **phospholipids** comprising 10 % phosphatidylethanolamine. (I) further comprises buffers and/or stabilizers, or **phospholipids.** Preferred Kit: The kit further comprises calcium **cation** or calcium salt that dissociates into a calcium **cation**, and an **activator** of an **anticoagulant pathway** and instruction for adding the **activator** to the test sample. The **thrombomodulin** is provided separately from the **coagulation activator**, and mixed with heparin, heparin sulfate or heparin-like molecules. The kit has a first container having the **coagulation activator** which is a **tissue factor** at a concentration of 11 picomolars or less mixed with **vesicles** which are **phospholipids** at a concentration of 10-300 picomolar, a second container having a metal salt at a concentration of 5-50 mM, and third container having the **coagulation activator** mixed with **vesicles** and an **activator** of an **anticoagulant pathway** which is **thrombomodulin** at a concentration of 300 nanomolar or less.

ABEX UPTX: 20020815

EXAMPLE - An assay was conducted for detecting the **coagulability**, by adding 50 micro-l of **plasma** to 50 micro-l of the **activator** and 50 micro-l of the start reagent which consisted of 0.25 M calcium chloride. A **normal** sample, a **hypocoagulable** sample (factor VIII deficient **plasma**) and a **hypercoagulable plasma** (protein S deficient **plasma**) were evaluated at various dilutions of the **activator.** The **activator** was diluted with a buffer at two dilutions, 1:100 and 1:50000 of its original concentration. The assay was conducted at 37 degrees C, and the reaction was monitored at 580 nm for 300 seconds. Endpoints were calculated for **time** and **rate** indices of **clot** formation. The **ratio** of the endpoint of reagent dilution (x) for specimen/endpoint of reagent dilution (y) for specimen to the endpoint of reagent dilution (x) for npp/endpoint of reagent dilution (y) for npp was calculated, where x is 1:100 dilution and y is a series of dilutions. The results were expressed as the magnitude of deviation at a given dilution or as the dilution required to deviate from ideal (**normal** value or **normal** range). As the dilution of the reagent was greater (y became larger) the results for the two abnormal **plasmas** (the **hypercoagulable** and **hypocoagulable plasmas**) tested began to deviate from the calculated endpoints or **ratios**

of the **normal plasma**. The **hypocoagulable** specimen produced **ratios** that were greater than 1 and the **hypercoagulable** specimen had **ratios** that were less than 1 for the endpoint (**clot time**)/**ratio** combination.

L62 ANSWER 4 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **2002-463332** [49] WPIX
DNN **N2002-365287** DNC **C2002-131735**
TI Determining hyper- or **hypocoagulable** condition of a patient, comprises **initiating coagulation** in patient sample by **fibrin polymerization activator** and monitoring formation of **fibrin polymer** to drive **time** dependent profile.
DC B04 D16 P31
IN **BAGLIN, T**; **FISCHER, T J**; **TEJIDOR, L**
PA (**ALKU**) **AKZO NOBEL NV**; (**INMR**) **BIOMERIEUX INC**; (BAGL-I) BAGLIN T; (FISC-I) FISCHER T J; (TEJI-I) TEJIDOR L
CYC 98
PI WO 2002034110 A2 20020502 (200249)* EN 68 A61B000-00 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2002014619 A 20020506 (200257) C12Q001-56 <--
EP 1337660 A2 20030827 (200357) EN C12Q001-56 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
BR 2001014936 A 20031007 (200373) C12Q001-00 <--
US 2004053351 A1 20040318 (200421) C12Q001-56 <--
US 6743596 B1 20040601 (200436) C12Q001-56 <--
JP 2004518111 W 20040617 (200440) 106 G01N033-86 <--
ADT WO 2002034110 A2 **WO 2001-US32564 20011018**; AU 2002014619 A AU 2002-14619 20011018; EP 1337660 A2 EP 2001-983170 20011018, **WO 2001-US32564 20011018**; BR 2001014936 A BR 2001-14936 20011018, **WO 2001-US32564 20011018**; US 2004053351 A1 Div ex US 2000-697934 20001027, **US 2003-663449 20030916**; US 6743596 B1 US 2000-697934 20001027; JP 2004518111 W **WO 2001-US32564 20011018**, JP 2002-537170 20011018
FDT AU 2002014619 A Based on WO 2002034110; EP 1337660 A2 Based on WO 2002034110; BR 2001014936 A Based on WO 2002034110; JP 2004518111 W Based on WO 2002034110
PRAI US 2000-697934 20001027; **US 2003-663449 20030916**
IC ICM **A61B000-00**; **C12Q001-00**; **C12Q001-56**; **G01N033-86**
ICS G01N021-75; **G01N033-15**; **G01N033-49**; **G01N033-50**
AB WO 200234110 A UPAB: 20020802
NOVELTY - Determining (M1) if a patient is **hypercoagulable**, **hypocoagulable** or **normal**, comprises **initiating coagulation** in the test sample of patient in the presence of an **activator** for carrying out intrinsic tenase-dependent **fibrin polymerization** (IP), and monitoring formation of IP over **time** to drive a **time**-dependent profile, where the results determine whether the patient is hyper- or **hypocoagulable**, or **normal**, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) assessing the **coagulation** system in a test sample;
(2) detecting defects in the propagation and/or amplification phase

in the **coagulation** system of a test sample;
(3) monitoring an **antithrombotic** or **procoagulant** pharmaceutical therapy;
(4) evaluating the efficacy of an **antithrombotic** or **procoagulant** pharmaceutical; and
(5) assessing the **hemostatic** potential of a sample.
ACTIVITY - **Thrombolytic**; **Anticoagulant**; **Coagulant**. No supporting data is given in the source material.
MECHANISM OF ACTION - None given in the source material.
USE - For determining if a patient is **hypercoagulable**, **hypocoagulable** or **normal**, for assessing the **coagulation** system in a test sample, monitoring an **antithrombotic** or **procoagulant** pharmaceutical therapy, evaluating the efficacy of an **antithrombotic** or **procoagulant** pharmaceutical and assessing **hemostatic** potential of a sample (claimed). The **method** is useful for assessing the **hemostatic** potential of a sample. The **method** is also useful for determining how much the **plasma** needs to be modified in order to restore **coagulability** to **normal**.
ADVANTAGE - The **method** allows for globally assessing both the **hypercoagulable** potential and **hypocoagulable** potential of a patient in a single assay. The **method** is accurate and easy to use. Disturbances in the propagation and amplification loops are accessible in this **method**, whereas in the traditional **prothrombin** (PT) test, the parts of the **coagulation** **pathway** are overshadowed by the excessive amounts of Factor IIa produced by the **initiation** phase.
Dwg.0/10

FS CPI GMPI
FA AB; DCN
MC CPI: **B04-B04D**; **B04-H19**; B11-C07B2; **B12-K04A2** ; **B14-F04**; **B14-F08**; **D05-H09**
TECH UPTX: 20020802
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **Method**: The **time**-dependent profile, at least part of which includes **initiation** of **clot** formation, overall change in profile, slope of profile after **initiation** of **clot** formation and/or acceleration at the **time** of **clot** **initiation**, is **compared** to a **time**-dependent profile of a known sample. At least two **time**-dependent **fibrin polymerization** profiles are obtained, an additional profile obtained for a known sample from computer memory or by adding the **activator** at least one concentration to a known sample and monitoring the formation of **fibrin** **polymerization** over **time**. At least two **time** -dependent **fibrin polymerization** profiles are obtained for two different **activator** concentrations, and/or one or more profiles for a known sample at one or more **activator** concentrations. Parameter from each **time**-dependent **fibrin polymerization** profile having varying **activator** concentrations is determined and a concentration at which at least one parameter of the sample being tested deviates from **normal** is determined. The parameter is the index and value of the minimum of first derivative, the **time** index and value for the minimum and maximum of the second derivative or overall magnitude of change. The part is **rate** of acceleration of **fibrin** **polymerization** **compared** to known sample. A difference or **ratio** of parameters for test sample and **normal** sample are determined. Parameter is **clot time** and a **ratio** of **clot times** at different **activator** concentrations is determined. The parameter includes the **time** of **initiation** of **clot** formation,

rate of **clot** formation, maximum acceleration of **clot** formation, **turbidity** at a predetermined **time** period or total change in **turbidity**. The parameters are measures of defects in the **thrombin** propagation and/or amplification phases. A **ratio** of one parameter in test and **normal** sample, and **ratio** for multiple concentrations of **activator**, are determined. A concentration at which **ratio** departs from 1 is determined. An **activator** of one or more **anticoagulant pathways**, and an **activator** of **protein C** e.g. **thrombomodulin** or its derivatives given in the specification are added. A **fibrin polymerization** profile is obtained with and without **thrombomodulin**. The **activator** comprises **tissue factor** and **phospholipids**. A metal salt (e.g. halide of magnesium, calcium or manganese) which dissociates into a metal divalent **cation** when added to the test sample, is added as part of the **activator**. The **activator** comprises homogenized cerebral tissue. M1 further involves adding phopholipids together with or separately from the **activator**, adding buffers and/or stabilizers to the test sample e.g. patient **plasma** sample. The **time** dependent measurement profile is an optical absorbance or transmittance profile provided on an automated analyzer. A visible light beam is directed through a container holding the test sample and **activator** , and light absorbed or transmitted is monitored to form the **time** dependent measurement profile. The **activator** comprises recombinant or purified **tissue factor**, truncated **tissue factor** or cells expressing **tissue factor** on their surface, sufficiently diluted to determine **hypercoagulable**, **normal** or **hypocoagulable** depending upon the condition of the patient. Defects in formation of intrinsic tenase complex are detected. One or more endpoints from the time-dependent measurement profile are calculated, the endpoints selected from the **time** of **clot initiation** and the **rate** of **polymerization**. Sample is whole **blood** or **platelet** rich **plasma**. M1 further involves adding **vesicles** (e.g. **platelets**, cellular debris, **phospholipid vesicles** or **platelet** microparticles) to the test sample. M1 further involves adding less than 11 pM concentration of **tissue factor** that generates intrinsic dependent **fibrin polymerization** in the patient sample, measuring formation of **fibrin polymerization**, and determining whether the patient is **hypercoagulable**, **normal** or **hypocoagulable**, based on the measured **fibrin polymerization**. **Fibrin polymerization** profile is obtained at multiple concentrations of **activator** which triggers **thrombin** explosion. The **fibrin polymerization** measurement is used to adjust the patient's therapy to result in a **fibrin polymerization** profile approximating **normal**.

ABEX UPTX: 20020802

EXAMPLE - The assay was conducted by adding 50 micro liter of **plasma** to 50 micro liter of the **activator** and then adding 50 micro liter of the start reagent. A **normal** sample, a **hypocoagulable** sample (Factor VIII deficient **plasma**) and a **hypercoagulable plasma** (protein S deficient **plasma**) were evaluated at various dilutions of the **activator**. The **activator** was a commercially available **thromboplastin** diluted with a buffer at two dilutions, a 1:100 and 1:500000 of its original concentration. The start reagent consisted of 0.25 M Calcium chloride. The assay was conducted at 37 degrees C and the reaction was monitored at 580 nm for 300 seconds. Endpoints were calculated for **time** and **rate** indices of **clot** formation. **Ratios** of endpoints were **compared** to other

dilutions and other samples. As the dilution of the reagent become greater, the results for the two abnormal **plasmas** (**hypercoagulable** and **hypocoagulable plasmas**) tested began to deviate from the calculated endpoints or **ratios** of the **normal plasma**. The results were expressed as the magnitude of deviation at a given dilution or as the dilution required to deviate from ideal (**normal** value or **normal** range). The **hypercoagulable** and **hypocoagulable** results deviating in opposite directions indicating the ability to differentiate between the two conditions, were shown graphically.

L62 ANSWER 5 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **2002-268645** [31] WPIX
DNN **N2002-209092** DNC **C2002-079631**
TI Assaying **activated protein C** in **blood**, for screening drugs, comprises contacting **plasma** with **blood coagulation** cascade **activator** and assaying activity of **activated protein C**.
DC B04 S03
IN HOSAKA, Y; IMADA, K; OHMORI, Y; SHIRAKAWA, K; TAKAHASHI, Y
PA (MOCH) MOCHIDA PHARM CO LTD
CYC 96
PI WO 2001098782 A1 20011227 (200231)* JA 49 G01N033-53 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001074597 A 20020102 (200233) G01N033-53 <--
JP 2002504491 X 20030916 (200362) G01N033-53 <--
ADT WO 2001098782 A1 WO 2001-JP5376 20010622; AU 2001074597 A AU 2001-74597 20010622; JP 2002504491 X WO 2001-JP5376 20010622, JP 2002-504491 20010622
FDT AU 2001074597 A Based on WO 2001098782; JP 2002504491 X Based on WO 2001098782
PRAI JP 2000-227966 20000622
IC ICM **G01N033-53**
ICS **C12Q001-56**; **G01N033-15**; **G01N033-50**; **G01N033-86**
ICA C12N009-99
AB WO 200198782 A UPAB: 20020516
NOVELTY - Assaying the amount of **activated protein C** in a **blood** sample comprising contacting **plasma** in a sample with a substance **activating** a **blood coagulation** cascade, and assaying the activity of an **activated protein C** and/or the amount of an antigen in a **protein C activated** protein, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a kit for conducting the above assay.
USE - The **method** is useful for assaying the amount of **activated protein C** in a **blood** sample (claimed) which can be used to screen drugs.
ADVANTAGE - Allows an assay of **protein C** to be conducted under conditions similar to physiological conditions.
Dwg.0/7
FS CPI EPI
FA AB; DCN
MC CPI: **B04-B04D2**; B04-C01; **B04-H19**; B04-N02; B11-C08E; B11-C10; B12-K04E; B14-L01; B14-L06
EPI: **S03-E14H4**
TECH UPTX: 20020516
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred **Method**: The

plasma in the **blood** sample is firstly contacted with a drug. The substance **activating** the **blood coagulation** cascade is **thromboplastin. Thrombin** activity inhibitor may be added just before the assaying step..

L62 ANSWER 6 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **2002-122222** [16] WPIX
DNN **N2002-091675** DNC **C2002-037464**
TI Detection of a complex of lipoprotein and an acute phase protein useful for predicting an increased probability of system failure or mortality involves adding a reagent to a sample, and measuring the formed complex over **time.**
DC B04 S03
IN DOWNEY, C; **FISCHER, T J**; NESHEIM, M; SAMIS, J A; **TEJIDOR, L**; TOH, C H; WALKER, J B
PA **(ALKU) AKZO NOBEL NV; (INMR) BIOMERIEUX INC**; (DOWN-I) DOWNEY C; (FISC-I) FISCHER T J; (NESH-I) NESHEIM M; (SAMI-I) SAMIS J A; (TEJI-I) TEJIDOR L; (TOHC-I) TOH C H; (WALK-I) WALKER J B
CYC 97
PI WO 2001096864 A2 20011220 (200216)* EN 83 G01N033-49 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001066795 A 20011224 (200227) G01N033-49 <--
US 2002193949 A1 20021219 (200303) G01N031-00
EP 1309857 A2 20030514 (200333) EN G01N033-49 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
BR 2001011987 A 20031028 (200374) G01N033-49 <--
JP 2004503254 W 20040205 (200412) 126 C12Q001-56 <--
ADT WO 2001096864 A2 WO 2001-US18611 20010608; AU 2001066795 A AU 2001-66795 20010608; US 2002193949 A1 WO 2001-US18611 20010608, US 2001-19087 20011219; EP 1309857 A2 EP 2001-944378 20010608, WO 2001-US18611 20010608; BR 2001011987 A BR 2001-11987 20010608, WO 2001-US18611 20010608; JP 2004503254 W WO 2001-US18611 20010608, JP 2002-510942 20010608
FDT AU 2001066795 A Based on WO 2001096864; EP 1309857 A2 Based on WO 2001096864; BR 2001011987 A Based on WO 2001096864; JP 2004503254 W Based on WO 2001096864
PRAI US 2000-591642 20000609; US 2001-19087 20011219
IC ICM **C12Q001-56**; G01N031-00; **G01N033-49**
ICS **G01N033-86**
AB WO 200196864 A UPAB: 20020308
NOVELTY - Detection of a complex of lipoprotein and an acute phase protein involves: adding at least one reagent to a test sample from a patient in order to cause formation of the complex; measuring the formation of the complex over **time** so as to derive a **time**-dependent measurement profile; and determining a slop and/or a **time** -dependent measurement profile so as to diagnose a condition of the patient.

DETAILED DESCRIPTION - Detection of a complex of at least one human lipoprotein and at least one acute phase protein involves:

(a) adding at least one reagent to a test sample from a patient comprising at least one part of a **blood** sample from the patient in order to cause formation of the complex, while causing no **fibrin polymerization**;

(b) measuring the formation of the complex over **time** so as to derive a **time**-dependent measurement profile; and

(c) determining a slope and/or a **time**-dependent measurement profile so as to diagnose a condition of the patient.

INDEPENDENT CLAIMS are also included for the following:
(1) predicting an increased probability of system failure or mortality of a patient involving: obtaining a **blood** sample from a patient, obtaining **plasma** or **serum** from the **blood** sample, adding the reagent, taking at least one measurement of a parameter of the **plasma** or **serum** and correlating the measured parameter to complex formation if present, and correlating the complex formation to the probability of system failure or mortality of the patient; and
(2) testing the effectiveness of a therapeutic involving:
(a) taking a test sample from a test subject;
(b) adding a reagent which causes formation of the complex in the test sample;
(c) administering to the subject a therapeutic;
(d) repeating the steps (a) and (b); and
(e) determining if the amount of complex formed has changed.
USE - For predicting an increased probability of system failure or mortality in a patient; diagnosing and treating patient with **hemostatic** dysfunction (claimed).
ADVANTAGE - The **method** detects particular abnormality and also monitors the progression of the disease in a single patient. The **method** is not only useful as early diagnostic and single monitoring marker of disseminated intravascular **coagulation** (DIC), but the quantifiable and standardizable changes also allow for prognostatic applicability in clinical management.
DESCRIPTION OF DRAWING(S) - The figures illustrate transmittance waveform, on the **activated** partial **thromboplastin time** (APTT) assay. Figure A shows a **normal** appearance, and (B) shows a biphasic appearance. The **clot time** is indicated by an arrow.
Dwg.1/50

FS CPI EPI
FA AB; GI; DCN
MC CPI: B04-N05; B11-C07; **B12-K04A2**
EPI: **S03-E14H; S03-E14H1**
TECH UPTX: 20020308

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Reagent: The reagent is metal ion (preferably divalent transition metal ion). The metal ion comprises at least one calcium, magnesium, manganese, iron or barium. Optionally a **clot** inhibitor is provided as part of the reagent or as part of an additional reagent added to the test sample. The reagent is capable of causing precipitate formation completely in the absence of **fibrin polymerization.** The precipitate inhibiting reagent comprises an apolipoprotein capable of binding to a lipoprotein-acute phase protein binding site. The precipitate inhibiting reagent is capable of inhibiting the association of C-reactive protein (CRP) with chylomicrons or their remnants, low density lipoprotein (LDL), very low density lipoprotein (VLDL) and/or intermediate density lipoprotein (IDL).

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred **Clot** Inhibitor: The **clot** inhibitor comprises at least one of hirudin, heparin, PPACK (RTM), I2581 (RTM) or **antithrombin.**
Preferred Process: The formation of the complex is correlated to the increase probability of death of the patient, greater the formation of the complex, the greater the probability of death of the patient. The **time**-dependent measurement profile is an optical transmission profile, and greater the decrease of optical transmittance through the test sample, greater the formation of the complex. Diagnosing of the condition of the patient involves a prediction of the probability of mortality of the patient. The formation of the precipitate is measured at least once after **time** t0. A single endpoint measurement is made of precipitate formation after **time** t0. The amount of

fibrin polymerization causes no change in optical transmittance. The **method** can also involve measuring a formation of a precipitate having the acute phase protein and the lipoprotein followed by addition of inhibiting reagent, before or after adding the precipitate causing reagent, which inhibits at least in part formation of the precipitate and determining the extent of inhibition of the inhibiting reagent. Several measurements are made after addition of the reagent in order to derive the **time**-dependent measurement profile. **Rate** of change of the measurements or a total change is determined and **hemostatic** dysfunction is determined based on the determined total and/or **rate** change. A single reagent is used prior to taking the measurements such as transmission or absorbance through the sample. The measurements are unaffected by **clot** formation due to lack of **fibrin polymerization.** The precipitate inhibiting reagent is either added after all or substantially all of the lipoprotein has become associated with acute phase protein so as to form the precipitate, or added prior to adding the precipitate causing reagent. Measurements are performed over **time** to derive **time** -dependent measurement profile. The formation of a complex and additional complex are measured over **time** to provide respective first and second **time**-dependent measurement profiles. The measured additional complex and measured initial complex together are correlated to a total amount of acute phase in the test phase. The formation of the complex can also be correlated to a concentration of the lipoprotein.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Components: The human lipoprotein comprises at least one chylomicrons or their remnants, VLDL, IDL, LDL or high density lipoprotein (HDL). The acute phase protein comprises C-reactive protein (CRP) and/or **serum** amyloid A (SAA) (preferably CRP).

Preferred Complex: A majority of the complex comprises CRP bound to VLDL.

ABEX UPTX: 20020308

EXAMPLE - Freshly collected **blood** samples requiring a **prothrombin** (PT) or **activated** partial **thromboplastin time** (APTT) were analyzed prospectively over a two week working period. The samples were taken in 0.105 M tri-sodium citrate in a **ratio** of 1 part **anticoagulant** to 9 parts whole **blood.** The **platelet**-poor **plasma** was analyzed on the multichannel discrete analyzer (MDA). The **clot time** were derived for PT (**normal** 11.2 - 15 seconds) using MDA simplastin LS (RTM) and APTT (**normal** 23-35 seconds) using MDA platelin LS (RTM) with 0.025 M calcium chloride. On analysis the transmittance waveform (TW) for APTT was performed at a wavelength of 580 nm. To ensure no cases of disseminated intravascular **coagulation** (DIC) were overlooked, a full DIC screen was performed to include the **thrombin time**; fibrinogen, and D-dimer levels on the Nyocard D-dimer (RTM). **Platelet** counts performed or an EDTA sample at the same **time** were recorded. A total of 1,470 samples from 747 patients were analyzed. 174 samples (11.9%) from 54 patients showed the bi-phasic waveform change. DIC was diagnosed in 41 patients with 30 of those requiring transfusion support with fresh frozen **plasma**, cryoprecipitate or **platelets.** 40 of the 41 patients with DIC showed the bi-phasic TW. The one false negative result (DIC without a bi-phasic TW) occurred in a patient with pre-eclampsia where the single sample showed a prolonged PT of 21 second, APTT of 44 seconds and raised D-dimer of 1.5 mg/liter. The results showed that the bi-phasic TW had a sensitivity of 97.6% and specificity of 98% for the diagnosis of DIC. The positive predictive value of the test was 74%, which increased with increasing steepness of the bi-phasic slope and decreasing levels of light transmittance.

L62 ANSWER 7 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-098089 [13] WPIX

CR 2000-572005 [53]; 2003-605936 [57]; 2003-615959 [58]; 2004-141748 [14]; 2004-224645 [21]
DNN N2002-072440 DNC C2002-030637
TI Measuring efficacy of anti-**platelet** agents, comprises determining **blood coagulation** parameters of **blood** samples obtained in the presence and absence of anti-**platelet** therapy, using **blood coagulation** analyzers.
DC B04 D16 S03
IN COHEN, E
PA (HAEM-N) HAEMOSCOPE CORP
CYC 97
PI WO 2001096879 A2 20011220 (200213)* EN 20 G01N033-86 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001075249 A 20011224 (200227)
EP 1287349 A2 20030305 (200319) EN G01N033-49 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 6613573 B1 20030902 (200359) G01N033-86 <--
CN 1436304 A 20030813 (200373) G01N033-49 <--
JP 2004503781 W 20040205 (200412) 34 G01N033-86 <--
ADT WO 2001096879 A2 WO 2001-US18154 20010605; AU 2001075249 A AU 2001-75249 20010605; EP 1287349 A2 EP 2001-941938 20010605, WO 2001-US18154 20010605; US 6613573 B1 CIP of US 1999-255099 19990222, US 2000-591371 20000609; CN 1436304 A CN 2001-810898 20010605; JP 2004503781 W WO 2001-US18154 20010605, JP 2002-510957 20010605
FDT AU 2001075249 A Based on WO 2001096879; EP 1287349 A2 Based on WO 2001096879; US 6613573 B1 CIP of US 6225126; JP 2004503781 W Based on WO 2001096879
PRAI US 2000-591371 20000609; US 1999-255099 19990222
IC ICM **G01N033-49**; **G01N033-86**
ICS A61K031-195; A61K031-197; A61K031-352; A61K031-727; A61K038-46; A61K038-48; A61P007-02; A61P007-04; **G01N033-15**
AB WO 200196879 A UPAB: 20040421
NOVELTY - Measuring (M) the efficacy of anti-**platelet** agents (A), involves determining a first **blood coagulation** parameter (P1) of a first **blood** sample obtained in the absence of anti-**platelet** therapy (AT) and determining a second **blood coagulation** parameter (P2) of a second **blood** sample in the presence of AT, using a **blood coagulation** analyzer (I), and determining the efficacy of (A) based on P1 and P2.

DETAILED DESCRIPTION - Measuring (M) the efficacy of anti-**platelet** agents (A), involves determining a first **blood coagulation** parameter (P1) of a first **blood** sample obtained in the absence of anti-**platelet** therapy (AT) and determining a second **blood coagulation** parameter (P2) of a second **blood** sample in the presence of AT, using a **blood coagulation** analyzer (I), and determining the efficacy of (A) based on P1 and P2. (I) is capable of measuring a **clot** strength in the range of about 100-1000 dyn/cm2.

An INDEPENDENT CLAIM is also included for an apparatus for measuring the efficacy of AT, which comprises:

(a) a **blood coagulation** analyzer (I) (10) operable to measure a first **blood** sample (13) in the absence of AT and a second **blood** sample in the presence of AT to respectively generate P1 and P2, where P1 and P2 are related to **blood clot** strength; and

(b) a processor having an associated control program for directing the operation of the processor for determining the efficacy of AT based upon P1 and P2.

USE - (I) and (M) are useful for measuring the efficacy of anti-**platelet** agents (claimed). The measured **blood coagulation** parameters permit confirmation of the attainment of therapeutic level of GPIIb/IIIa receptor blockade, individualized dosing assessment to evaluate attainment of adequate GPIIb/IIIa receptor blockage, individualized dosing assessment required to reach adequate GPIIb/IIIa receptor blockade, illustration of the **rate** of diminishment of **platelet** inhibition or inhibition recovery after treatment with **platelet**-inhibition drugs, evaluation of the interaction effect of a combination of **thrombolytic** or any other agents or conditions effecting hemostasis and **platelet** -inhibiting agents on patient hemostasis.

ADVANTAGE - The **blood coagulation** analyzer is utilized to measure continuously in real **time**, the **clotting** process from the initial **fibrin** formation, through **platelet fibrin** interaction and lysis to generate **blood coagulation** parameters.

DESCRIPTION OF DRAWING(S) - The figure shows the **blood coagulation** analyzer.

Blood coagulation analyzer 10

Blood sample 13

Dwg.2/4

FS CPI EPI

FA AB; GI; DCN

MC CPI: **B04-B04D5; B04-F04; B04-H19;** B11-C08; **B14-F04; D05-H09**

EPI: **S03-E14H**

TECH UPTX: 20020226

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **Method**:

Determination of P1 involves:

(a) testing a sampled portion of the first **blood** sample to determine a first characteristic; and

(b) testing a portion of the first **blood** sample treated in vitro to inhibit **thrombin activation**, and to preserve fibrinogen and **platelet activation** to determine a second characteristic.

Determination of P2 involves:

(a) testing a sampled portion of the second **blood** sample to determine a first characteristic; and

(b) testing a portion of the second **blood** sample treated in vitro to inhibit **thrombin activation**, and to preserve fibrinogen and **platelet activation** to determine a second characteristic.

(M) is performed in conjunction with administration of at least one of the **blood coagulation** therapies including:

(i) anti-**coagulation** therapy utilizing the administration of heparin or warfarin;

(ii) **thrombolytic** therapy utilizing the administration of tPA, steptokinase and urokinase;

(iii) anti-fibrinolytic therapy utilizing e-amino-caproic acid, trasylol and tranexamic acid;

(iv) anti-**platelet** therapy and a **blood** component transfusion therapy.

(M) is performed in connection with assessment of **thrombotic** risk, **hypercoagulable** condition or **hypocoagulable** condition. P1 and P2 are based upon the latency period of **clot** formation, **rate** of **clot** formation, maximum **clot** strength or **rate** of **clot** lysis. P1 and P2 correspond to an estimate of **fibrin-platelet** interaction. P1 is represented by a first maximum amplitude measurement

and P2 is represented by a second maximum amplitude measurement, and (M) involves **comparing** the amplitudes.
Preferred Apparatus: (I) provides for the substantially simultaneous testing of the first and second **blood** samples.

ABEX UPTX: 20020226
EXAMPLE - None given.

L62 ANSWER 8 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-091713 [13] WPIX
DNN N2002-067550 DNC C2002-028520
TI Testing system for **coagulation** promoting substance has sample wells for measuring test **clotting** indicator **time** of patient's **blood** and **coagulation** promoting substance as test sample, and of patient's **blood** as control sample.
DC B04 D16 S03
IN GOLDSTEIN, S
PA (GOLD-I) GOLDSTEIN S
CYC 28
PI EP 1162457 A2 20011212 (200213)* EN 17 G01N033-49 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
AU 2001051826 A 20011213 (200213) G01N035-02
CA 2349959 A1 20011209 (200213) EN G01N033-86 <--
ADT EP 1162457 A2 EP 2001-202205 20010608; AU 2001051826 A AU 2001-51826 20010608; CA 2349959 A1 CA 2001-2349959 20010608
PRAI US 2000-591329 20000609
IC ICM **G01N033-49**; **G01N033-86**; G01N035-02
ICS **C12Q001-56**
AB EP 1162457 A UPAB: 20020226
NOVELTY - An automated multiple **coagulation** testing system has sample wells for measuring a test **clotting** indicator **time** of the patient's **blood** and **coagulation** promoting substance as a test sample; and for measuring a baseline **clotting** indicator **time** of the patient's **blood** as a control sample. An appropriate therapy is determined by **comparing clotting** indicator **time** of control sample and test sample.

DETAILED DESCRIPTION - An automated multiple **coagulation** testing system includes at least three sample wells for receiving patient's **blood** (35), at least two other sample wells (75A-D) for measuring a test **clotting** indicator **time** of the patient's **blood** and **coagulation** promoting substance (105A) as a test sample. At least one of the sample wells (75-E) is for measuring a baseline **clotting** indicator **time** of the patient's **blood** as a control sample. The control sample wells are free of **coagulation** promoting substance. The test sample wells (95A-D) each contain a different **coagulation** promoting substance. The **coagulation** substance is an agent or combination of agents capable of improving **clotting** function in the patient. The sample wells are constructed and arranged to allow detection of a **clotting** indicator in the patient's **blood** for measuring **clotting** indicator **time**. An appropriate therapy for improving **clotting** function in the patient is determined by **comparison** of the baseline **clotting** indicator time of the control sample with the test **clotting** indicator **time** of the patient's **blood** and the **coagulation** promoting substance.

An INDEPENDENT CLAIM is also included for a **method** of determining an appropriate **coagulation** promoting substance for administration to a patient as a therapy for improving **clotting** function involving adding a selected amount of a patient's **blood** to each of the at least three sample wells, and adding a different **coagulation** promoting substance to each of the test sample wells.

USE - For determining an appropriate **coagulation** promoting substance for administration to a patient as a therapy for improving **clotting** function.

ADVANTAGE - The system produces results indicating a proper course treatment without resort to a shotgun approach, which requires an addition of multiple agents to a patient and thus avoids several of the complications inherent in using such approach. The system thus allows rapid determination of a specific treatment in a **hemorrhaging** situation without awaiting **standard** laboratory test results.

DESCRIPTION OF DRAWING(S) - The figure shows a schematic view of the testing system.

Blood 35

Sample wells for measuring test **clotting** indicator **time** of test sample 75A-D

Sample well for measuring baseline **clotting** indicator **time** of control sample 75-E

Sample wells containing **coagulation** promoting substance 95A-D

Coagulation promoting substance 105A-D

Coagulation detector 125A-E

Dwg.2/2

FS CPI EPI

FA AB; GI; DCN

MC CPI: **B04-B04D**; **B04-H19**; B04-H20A; B11-C07B4; B11-C08E; B12-K04E; **D05-H09**

EPI: **S03-E14H**; **S03-E14H1**

TECH UPTX: 20020226

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Component: The sample wells include tubes for containing the **blood**, and filter paper for receiving the **blood.** The system has a magnetic rod in each of the tubes, and a magnetic detector (125A-E) triggerable by displacement of the magnetic rods. It has a light source, a photo-optical detector, a viscometer, holder for containing a patient's **blood**, an aliquot meter connected with the holder for withdrawing a predetermined measured amounts of the patient's **blood**, and dosing meters connected with the test sample wells for withdrawing a preselected equivalent dose of the **coagulation** promoting substances from the test sample wells. The holder is removably attached in connection with the aliquot meter. The test sample wells are removably attached in connection with the dosing meters. Each well contains diatomaceous powder for increasing the surface area for contact of substances involved in **clotting.** There are 4-10 wells used.

Preferred Mechanism: The **clotting** indicator is detected by the magnetic detector when displacement of the magnetic rods due to **blood clotting** occurs in any of the tubes, or when a change of light transmission from the light source to the detector due to **blood clotting** occurs in any of the sample wells. The **clotting** indicator is detected by the viscometer when a change of viscosity due to **blood clotting** occurs in the sample wells.

Preferred Substance: The **coagulation** promoting substance is **coagulation** factors, recombinant **coagulation** factors, bovine **coagulation** factors, **coagulation** factor VIII:C, von Willebrand factor, **platelets**, fibronectin, **thrombin**, desmopressin acetate, epsilo-amino caproic acid, cryoprecipitate, fresh frozen **plasma**, protamine, aprotinin or calcium ion. The **coagulation** factor is **coagulation** factor I (fibrinogen), Ia (**fibrin**), II (**prothrombin**), IIa (**thrombin**), III (**thromboplastin**), or IV-XIII, preferably recombinant factor VIII. The cryoprecipitate is bovine or human cryoprecipitate. The fresh frozen **plasma** is bovine or human fresh frozen **plasma.** The **coagulation** inhibiting substance is heparin, aprotinin, carbacyclin, prostacyclin, prostaglandin E1, or abciximab.

L62 ANSWER 9 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-075349 [10] WPIX
DNN N2002-055548 DNC C2002-022532
TI Inducing or reducing hemostasis in a subject for treating **hypocoagulation** disorders, vasculature-associated diseases and **thrombotic** disorders, comprises administering to the subject a modulator of P-selectin activity.
DC B04 D16 S03
IN ANDRE, P; HARTWELL, D W; HRACHOVINOVA, I; WAGNER, D D
PA (BLOO-N) CENT BLOOD RES; (BLOO-N) CENT BLOOD RES INC; (ANDR-I) ANDRE P; (HART-I) HARTWELL D W; (HRAC-I) HRACHOVINOVA I; (WAGN-I) WAGNER D D
CYC 97
PI WO 2001089564 A2 20011129 (200210)* EN 93 A61K039-395
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001061735 A 20011203 (200221) A61K039-395
US 2002031508 A1 20020314 (200222) A61K038-48
EP 1289552 A2 20030312 (200320) EN A61K039-395
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
JP 2003534291 W 20031118 (200401) 108 A61K045-00
ADT WO 2001089564 A2 WO 2001-US16021 20010517; AU 2001061735 A AU 2001-61735 20010517; US 2002031508 A1 Provisional US 2000-205734P 20000519, US 2001-860618 20010517; EP 1289552 A2 EP 2001-935660 20010517, WO 2001-US16021 20010517; JP 2003534291 W JP 2001-585806 20010517, WO 2001-US16021 20010517
FDT AU 2001061735 A Based on WO 2001089564; EP 1289552 A2 Based on WO 2001089564; JP 2003534291 W Based on WO 2001089564
PRAI US 2000-205734P 20000519; US 2001-860618 20010517
IC ICM A61K038-48; A61K039-395; A61K045-00
ICS A61K035-14; A61K038-00; A61K038-17; A61K048-00; A61P007-00; A61P007-02; A61P007-04; A61P009-00; A61P009-10; A61P035-00; A61P043-00; **G01N033-50**; **G01N033-68**; **G01N033-86**
AB WO 200189564 A UPAB: 20020213
NOVELTY - Inducing (M1) or reducing hemostasis in a subject, comprising administering an inducer or inhibitor of P-selectin activity, a soluble P-selectin polypeptide (I), an isolated polynucleotide comprising a sequence encoding (I), a recombinant cell expressing (I), or an isolated nucleic acid molecule comprising a sequence antisense to a sequence encoding (I), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) modulating (M2) **hemostatic** potential in a subject, involves modulating P-selectin activity in the subject;

(2) diagnosing (M3) a **procoagulant** state in a subject, involves determining a P-selectin activity in a biological sample of the subject, where an increased P-selectin activity in the sample indicates a **procoagulant** state in the subject;

(3) identifying (M4) a subject having a **thrombotic** disorder, or at risk for developing a **thrombotic** disorder, comprising determining P-selectin activity in a biological sample of the subject, where an increased P-selectin activity in the sample identifies a subject having a **thrombotic** disorder, or at risk for developing a **thrombotic** disorder;

(4) identifying (M5) a compound capable of modulating hemostasis, comprising:

(a) assaying the ability of the compound to modulate a P-selectin

activity; and

(b) identifying a compound capable of modulating hemostasis;

(5) a pharmaceutical composition (II) for modulating hemostasis comprising a compound identified by M5; and

(6) a pharmaceutical composition (III) for modulating hemostasis containing at least one compound which is a modulator of P-selectin activity.

ACTIVITY - **Hemostatic**; antitumor; antiarteriosclerotic; **thrombolytic**; antianginal; vasotropic; antidiabetic; ophthalmological; antipsoriatic; dermatological; antiinflammatory; antiallergic; cytostatic; gynecological; antirheumatic; antiarthritic; cerebroprotective; cardiant; cytostatic. delta CT mice were treated with soluble P-selectin (PSGL)-Ig. Soluble PSGL-Ig infusion decreased the pro-**coagulant** phenotype of delta CT mice as shown by a significant decrease in the number of microparticles and a prolonged **clotting time** of **plasma**. Infusion of control Ig had no such effect. The **clotting time** was significantly longer in mice treated with soluble PSGL-Ig than in control Ig treated group.

MECHANISM OF ACTION - Modulator of hemostasis (claimed). No biolgical data provided.

USE - M1 is useful for modulating hemostasis in a subject. M1 is useful for treating or preventing a disorder (such as **hemorrhagic** disorder or hemophilia) associated with **hypocoagulation** in a subject, by administering to the subject an inducer of P-selectin activity or (I)1, such that the disorder associated with **hypocoagulation** is treated or prevented. M1 is useful for treating a vasculature-associated disease such as tumor in a subject, by administering an inducer of P-selectin activity or (I), to the subject. The subject is further treated with a molecule effective to induce a **procoagulant** state in tumor associated vasculature. The molecule comprises a first binding region that binds to a component of a tumor cell or tumor associated vasculature, operatively linked to a **coagulation** factor or a second binding region that binds to a **coagulation** factor. The first binding region comprises an antibody or its fragment, that binds to VCAM-1, operatively linked to **tissue factor**. M1 is useful for treating or preventing a **thrombotic** disorder in a subject, by administering to the subject an inhibitor of P-selectin activity, such that the **thrombotic** disorder is treated or prevented. The **thrombotic** disorder is arteriosclerosis, deep vein **thrombosis**, angina or restenosis following medical intervention (claimed). M1 is useful for treating disorders resulting from a deficiency in **clotting** factors or **platelet** ligands, e.g., a deficiency in von Willebrand's factor resulting in von Willebrand's disease, vasculature-associated diseases such as benign and malignant tumors or growth, diabetic retinopathy, vascular restenosis, neovascular glaucoma, psoriasis, synovitis, dermatitis, endometriosis, angiofibroma, rheumatoid arthritis, atherosclerotic plaques, corneal graft neovascularization, hemophilic joints, hypertrophic scars, and Osler-Weber syndrome, and **thrombotic** disorder such as **thromboembolism**, stroke, myocardial infarction, inflammatory disorders, cancer metastasis or sickle cell disease.

Dwg.0/14

FS CPI EPI

FA AB; DCN

MC CPI: **B04-B04D5**; B04-C01; B04-E03F; B04-E06; B04-F0100E; B04-N02; B11-C08E; **B12-K04A2**; B14-F01D; B14-F01G; **B14-F04**; B14-F07; **B14-F08**; B14-H01B; D05-C07; D05-C11; **D05-H09**; D05-H12A; D05-H12D2; D05-H14B2; D05-H17A6

EPI: **S03-E14H**

TECH UPTX: 20020213

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **Method**: In M1, the inducer of P-selectin activity increases the level of (I) in the **plasma** of the subject, increases the proteolytic cleavage of

P-selectin from a cell surface or increases P-selectin gene expression. The inducer of P-selectin activity binds to a P-selectin receptor or ligand and mimics the activity of a P-selectin polypeptide. The inducer of P-selectin activity is an antibody to a P-selectin receptor of ligand, where the antibody or ligand is PSGL-1. The inhibitor of P-selectin activity decreases the level of soluble P-selectin polypeptide in the **plasma** of the subject, decreases the proteolytic cleavage of P-selectin from the cell surface, or decreases P-selectin gene expression. The inhibitor of P-selectin activity is an anti-P-selectin antibody, or a recombinant soluble PSGL-1. In M2, modulating involves administering to the subject a modulator of P-selectin activity, where the modulator regulates the level of soluble P-selectin in the **plasma** of the subject. M3 involves providing a test sample of **blood** from a subject and **comparing** the level of soluble P-selectin in the test sample to the level of soluble P-selectin in a control **blood** sample from a subject with **normal hemostatic** activity, where an increased level of soluble P-selectin in the test samples as **compared** to the control sample is an indication of a **procoagulant** state in the subject. M4 involves contacting a sample of **blood** obtained from the subject with a P-selectin binding substance, and detecting the presence of increased levels of soluble P-selectin in the sample, thus identifying a subject having a **thrombotic** disorder, or at risk for developing a **thrombotic** disorder. In M5, the P-selectin activity is the expression of soluble P-selectin.

ABEX UPTX: 20020213

WIDER DISCLOSURE - Also disclosed as new, is an active agent which modulates soluble P-selectin expression or activity.

ADMINISTRATION - Administration is parenteral, intravenous, intradermal, subcutaneous, oral, by inhalation, transdermal, topical, transmucosal or rectal. Dosage is 0.001-30 mg/kg body weight, preferably 5-6 mg/kg body weight.

EXAMPLE - No relevant example is given.

L62 ANSWER 10 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-316462 [33] WPIX
DNN N2001-227460 DNC C2001-097551
TI Monitoring the effect of Factor Xa inhibitors, comprises collecting **plasma** sample from patient, who has received FXa inhibitor, an **anticoagulant**, an **antithrombotic** agent, adding solution of Russell's viper venom to **plasma** sample.
DC B04 S03
IN FUNG-HWEI, V C; CHU, V F
PA (AVET) AVENTIS PHARMA DEUT GMBH; (CHUV-I) CHU V F
CYC 95
PI WO 2001033217 A2 20010510 (200133)* EN 11 G01N033-50 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001015157 A 20010514 (200149) G01N033-50 <--
EP 1230382 A2 20020814 (200261) EN C12Q001-56 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 2003049704 A1 20030313 (200321) C12Q001-56 <--
JP 2003513280 W 20030408 (200333) 19 G01N033-86 <--
EP 1230382 B1 20040526 (200435) EN C12Q001-56 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 2001033217 A2 WO 2000-EP10646 20001028; AU 2001015157 A AU 2001-15157

20001028; EP 1230382 A2 EP 2000-977438 20001028, WO 2000-EP10646 20001028; US 2003049704 A1 Cont of WO 2000-EP10646 20001028, US 2002-125627 20020418; JP 2003513280 W WO 2000-EP10646 20001028, JP 2001-535051 20001028; EP 1230382 B1 EP 2000-977438 20001028, WO 2000-EP10646 20001028

FDT AU 2001015157 A Based on WO 2001033217; EP 1230382 A2 Based on WO 2001033217; JP 2003513280 W Based on WO 2001033217; EP 1230382 B1 Based on WO 2001033217

PRAI GB 1999-30535 19991223; US 1999-163161P 19991102

IC ICM **C12Q001-56**; **G01N033-50**; **G01N033-86**
ICS **G01N033-15**

AB WO 200133217 A UPAB: 20010615
NOVELTY - A **method** of monitoring the effect of Factor Xa (FXa) inhibitors comprising:
(a) collecting a **plasma** sample from a patient, who has received a FXa inhibitor, an **anticoagulant**, an **antithrombotic** agent, or any combination;
(b) adding a solution of Russell's viper venom to the **plasma** sample and
(c) measuring **clotting time** or a chromogenic change.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a **method** of monitoring the effect of Factor Xa inhibitors comprising of:
(a) collecting a **plasma** sample from a mammal;
(b) providing a Factor X deficient **plasma** sample of the same species to be used to make serial dilutions of the **normal plasma** sample;
(c) adding a solution of Russell's viper venom to the **plasma** samples;
(d) **comparing** the **clotting time** measured for the **plasma** sample with the **clotting time** measured for the **plasma** samples diluted with Factor X deficient **plasma**;
(e) constructing a **standard** curve of % FXa activity (proportional to the **normal plasma** content) and **clotting time** prolongation; and
(f) knowing the **clotting time** of the mammal, which received FXa inhibitor treatment, % residual FXa activity or % FXa inhibition is obtained from the **standard** curve;
(2) a **method** of monitoring the effect of Factor Xa inhibitors comprising:
(a) collecting a **plasma** sample from a mammal;
(b) dividing the **plasma** sample into portions, saving one portion as the control **normal plasma** and adding serial dilutions of Factor Xa inhibitor to other portions;
(c) adding a solution of Russell's viper venom to **plasma** samples defined in (b);
(d) **comparing** the **clotting time** measured for the **plasma** sample without Factor Xa inhibitor with that **plasma** samples with added Factor Xa inhibitor;
(e) constructing a dose-dependent **clotting time** prolongation curve and determining the concentration of a FXa inhibitor required to prolong the **clotting time** twice longer than the control **plasma clotting time**; and
(3) a **method** of monitoring the effect of Factor Xa inhibitors comprising:
(4) collecting a **plasma** sample from a mammal;
(a) dividing said **plasma** sample into portions, saving one portion as the control **plasma** and adding serial dilutions of Factor Xa inhibitor to other portions;
(b) adding a solution of Russell's viper venom (RVV-X) to **plasma** samples defined in (b);

(c) **comparing** the FXa activity measured for the control **plasma** with the residual FXa activity measured for the other **plasma** samples with added Factor Xa inhibitor;

(d) constructing a **standard** curve of dose-dependent inhibition of RW-X induced by FXa inhibitor; and

(e) the concentration of FXa inhibitor is estimated by using the **standard** curve.

USE - Russell's viper venom-induced **plasma** factor Xa monitors the safety and efficacy of intravenous or orally active FXa inhibitors, **thrombin** inhibitors and indirect FXa inhibitors such as **anticoagulants** for factors upstream of the **coagulation** cascade and heparin, more particularly low molecular weight heparin.

ADVANTAGE - None given.

Dwg.0/0

FS CPI EPI

FA AB; DCN

MC CPI: **B04-B04D4**; B04-B04G; **B04-H19**; B07-D04; B11-C08E; B11-C08E2; B12-K04A; B12-K04E; **B14-F08**; B14-L01; B14-L06

EPI: **S03-E14H**

TECH UPTX: 20010615

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred **Method**: The residual FXa activity is measured chromogenically. Cephalin is added to the **plasma** samples. The **plasma** samples were incubated in a buffer having a pH from 7 - 8.

Preferred Inhibitor: The FXa inhibitor is methyl-3-(4'-Noxopyridylphenoyl)-3-methyl-2-(m-amidinobenzyl)-propionate.

L62 ANSWER 11 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2001-315989 [33] WPIX

DNN N2001-227171 DNC C2001-097248

TI Quantitative determination of soluble **fibrin** in opaque sample, useful for early detection of disseminated intravascular **coagulation**, by determining **time** taken to detect **fibrin** precipitate.

DC B04 D16 S03

IN BULL, B S; KORPMAN, R A; HAY, K L

PA (MEDI-N) MEDICAL DEVICES CORP

CYC 95

PI WO 2001016360 A1 20010308 (200133)* EN 22 C12Q001-56 <--

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000073431 A 20010326 (200137) C12Q001-56 <--

EP 1214448 A1 20020619 (200240) EN C12Q001-56 <--

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

US 6436655 B1 20020820 (200257) C12Q001-56 <--

JP 2003508060 W 20030304 (200319) 20 C12Q001-56 <--

US 2003059836 A1 20030327 (200325) G01N033-53 <--

ADT WO 2001016360 A1 WO 2000-US24106 20000901; AU 2000073431 A AU 2000-73431 20000901; EP 1214448 A1 EP 2000-961486 20000901, WO 2000-US24106 20000901; US 6436655 B1 CIP of US 1998-21062 19980209, US 1999-388796 19990902; JP 2003508060 W WO 2000-US24106 20000901, JP 2001-520905 20000901; US 2003059836 A1 CIP of US 1998-21062 19980209, Cont of US 1999-388796 19990902, US 2002-136037 20020429

FDT AU 2000073431 A Based on WO 2001016360; EP 1214448 A1 Based on WO 2001016360; JP 2003508060 W Based on WO 2001016360; US 2003059836 A1 Cont of US 6436655

PRAI US 1999-388796 19990902; US 1998-21062 19980209;

US 2002-136037 20020429
IC ICM **C12Q001-56**; **G01N033-53**
ICS C07K007-08; **C12Q001-37**; **G01N033-49**; **G01N033-86**
AB WO 200116360 A UPAB: 20010615
NOVELTY - Determining (M1) the existence and the amount of soluble **fibrin** (SF) contained in an opaque specimen fluid is new.
DETAILED DESCRIPTION - (M1) comprises:
(1) mixing a portion of the opaque specimen fluid in a transparent container with a sufficient amount of precipitating reagent under a condition to cause the soluble **fibrin** to precipitate;
(2) aggregating and concentrating the soluble **fibrin** precipitates in a region of the container for rendering the precipitates optically detectable in the opaque specimen fluid;
(3) optically detecting the precipitates; and
(4) recording the **time** when the precipitates are first become optically detectable in the opaque specimen fluid, where the **time** elapsed from the addition of the precipitating reagent to the detection of the aggregated precipitates is an inverse measure of the quantity of soluble **fibrin** present in the opaque specimen fluid.
USE - The **method** is particularly used to detect SF during major surgery or in cases of severe trauma, where disseminated intravascular **coagulation** (DIC) is a risk. SF is a sensitive indicator of early DIC.
ADVANTAGE - The **method** is rapid and quantitative, and can be performed on whole **blood**, i.e. in the operating theater without need for separation of **plasma**, allowing immediate action to be taken to combat DIC. By collecting precipitate in a selected region of the container, the precipitate can be detected optically, even in opaque samples.
Dwg.0/3
FS CPI EPI
FA AB; DCN
MC CPI: **B04-B04D5**; B04-B04H; B04-C03; B04-N02; B11-C07B2; B11-C08D3; B11-C09; B12-K04A; **D05-H09**; D05-H13
EPI: S03-E09; **S03-E14H1**
TECH UPTX: 20010615
TECHNOLOGY FOCUS - BIOLOGY - Preferred Process: The **time** at which the precipitate sticks to, and rotates with, the container is also measured; it also is inversely related to SF content. Step (ii) particularly involves placing the container in a rocking/rotating device. The measured **time** is **compared** with a **standard** curve, produced by analyzing samples of known SF contents. The **time** is determined e.g. by direct visual examination, using a charge-coupled device camera etc. Optionally a second portion of the sample is tested separately, using either a different precipitant or a different concentration of the same precipitant, the result processed as above and an average value of the two determinations taken. Preferred Sample: This is whole **blood**, a bloody effusion or a bloody cerebrospinal fluid sample, preferably diluted with buffer (pH 5-9) and processed at 37 degrees centigrade.
Preferred Precipitant: This is protamine sulfate and/or polybrene.
ABEX UPTX: 20010615
EXAMPLE - **Blood** samples (150 microliter) were taken at 30 min intervals from a subject undergoing a liver transplant operation. Samples were diluted with saline (450 microliter) then treated with protamine sulfate (20 microliter) and the mixture placed in a **hemostatic** analyzer that rocked and rotated the sample. The sample was kept at 37 degrees centigrade and the **time** at which precipitate was first visible was taken as the first end point and the **time** at which the precipitate adhered to, and rotated with, the container was taken as the second end point. The level of soluble **fibrin** (SF) was below 20 units during the early stages of the operation but increased sharply,

to about 70 units, during the anhepatic stage, followed by a slight decline. The SF level was strongly positively correlated with levels of both **fibrin** degradation products and D-dimer, also strongly negatively correlated with levels of fibrinogen.

L62 ANSWER 12 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **2001-234924** [24] WPIX
CR 1997-052574 [05]; 1999-458146 [38]; 2000-514997 [46]; 2001-091718 [10]; 2002-147005 [19]
DNC **C2001-070340**
TI Detecting presence of **hemostatic** dysfunction, useful e.g. for diagnosing or monitoring of disseminated intravascular **coagulation**, by precipitation without **fibrin polymerization.**
DC B04
IN DOWNEY, C; **FISCHER, T J**; TOH, C H
PA (**ALKU**) **AKZO NOBEL NV**; (DOWN-I) DOWNEY C; (FISC-I) FISCHER T J; (TOHC-I) TOH C H; (**INMR**) **BIOMERIEUX SA**
CYC 24
PI WO 2001013125 A1 20010222 (200124)* EN 91 G01N033-86 <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP KR US
AU 2000066179 A 20010313 (200134) G01N033-86 <--
EP 1200837 A1 20020502 (200236) EN G01N033-86 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 6429017 B1 20020806 (200254) G01N033-86 <--
KR 2002021811 A 20020322 (200264) G01N033-86 <--
JP 2003507713 W 20030225 (200317) 67 G01N033-86 <--
US 2003049851 A1 20030313 (200321) G01N033-86 <--
ADT WO 2001013125 A1 WO 2000-US21022 20000802; AU 2000066179 A AU 2000-66179 20000802; EP 1200837 A1 EP 2000-953788 20000802, WO 2000-US21022 20000802; US 6429017 B1 CIP of US 1999-244340 19990204, US 1999-372954 19990812; KR 2002021811 A KR 2002-701897 20020209; JP 2003507713 W WO 2000-US21022 20000802, JP 2001-517176 20000802; US 2003049851 A1 Cont of US 1995-477839 19950607, CIP of US 1997-859773 19970521, CIP of US 1997-1647 19971231, CIP of US 1999-244340 19990204, Div ex US 1999-372954 19990812, US 2002-156462 20020528
FDT AU 2000066179 A Based on WO 2001013125; EP 1200837 A1 Based on WO 2001013125; JP 2003507713 W Based on WO 2001013125; US 2003049851 A1 Cont of US 5708591, CIP of US 6101449, CIP of US 6321164, Div ex US 6429017
PRAI US 1999-372954 19990812; US 1999-244340 19990204;
US 1995-477839 19950607; US 1997-859773 19970521;
US 1997-1647 19971231; US 2002-156462 20020528
IC ICM **G01N033-86**
ICS A61P007-04; **G01N033-15**; **G01N033-48**; **G01N033-50**; **G01N033-53**
AB WO 200113125 A UPAB: 20030603
NOVELTY - **Method** comprising treating a test sample, containing at least one component of **blood**, with a reagent (R) then measuring formation of a precipitate (P) over **time** to produce a **time**-dependent measurement profile. (R) forms a precipitate without significant **polymerization** of **fibrin.**

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) determining presence of a complex (C) of proteins, comprising at least one of **serum** amyloid A and C-reactive protein (CRP);

(2) **methods** for determining possibility or probability of **hemostatic** dysfunction;

(3) **method** for monitoring an inflammatory condition using (R);

(4) **method** for diagnosing or treating **hemostatic** dysfunction (HD) using (R);

(5) immunoassay for diagnosing HD by detecting or quantifying CRP or a 300 kD protein (I); and

(6) **method** for testing new drugs on humans or animals having an inflammatory condition and/or HD.

ACTIVITY - **Anticoagulant**; **Antithrombotic**; Antiarthritic; Antiinflammatory; Antibacterial; Immunosuppressive; Antirheumatic.

MECHANISM OF ACTION - None given.

USE - (R) is used

(i) to diagnose **hemostatic** dysfunction (HD), particularly disseminated intravascular **coagulation** (DIC) or a condition that can lead to DIC, bleeding or **thrombosis**, also to optimize and monitor treatment,

(ii) to monitor an inflammatory condition (rheumatoid arthritis, sepsis or conditions caused by surgical trauma) or

(iii) to screen for new drugs for treatment of HD or inflammation.

ADVANTAGE - The **method** provides early indication of disseminated intravascular **coagulation**, and since it can be standardized and made quantitative, it is suitable for prognosis and monitoring. It is simple and provides results quickly.

Dwg.0/29

FS CPI

FA AB; DCN

MC CPI: **B04-B04D4**; **B04-B04D5**; B04-N02; B05-A01B; B05-A03A; B11-C07A; **B12-K04A2**; B14-A01; B14-C03; B14-C09B; **B14-F04**; B14-G02; B14-S12

TECH UPTX: 20010502

TECHNOLOGY FOCUS - BIOLOGY - Preferred reagent: (R) contains a metal ion, preferably divalent, and especially calcium, magnesium, manganese, iron or barium. It may also include a **clotting** inhibitor (CI), e.g. hirudin, heparin, PPACK, I2581 or **antithrombin**, or CI is provided in another reagent. (R) causes formation of (P) completely in absence of **fibrin polymerization.** Preferred precipitate: (P) comprises a protein of about 20 kD that is insoluble in saline, ethylenediamine tetraacetic acid or imidazole but soluble in 5 M urea. Preferred process: The formation of (P) is correlated with HD, with increased amounts of (P) indicating more severe dysfunction, and this can be quantified by constructing a reference curve for **comparison** with the patient sample. Especially the profile is an optical transmission or absorbance profile, with a greater reduction in transmission indicating a greater formation of (P). If any **fibrin polymerization** does occur, then it does not cause a change in optical transmittance. (R) is added in absence of **clot**-inducing reagents and either a single (end-point) measurement is made or several measurements, in which case HD is detected from the **rate** of change. The test sample is particularly **plasma** and the test may be repeated at different (R)/**plasma ratios** or at different **times** (to monitor progression or regression of disease). In **method** (a), a test sample (preferably **blood** or a **blood** component) is treated with an alcohol (especially (m)ethanol), CI and metal **cation.** The precipitate forms contains (C). In **method** (b), a **coagulation** reagent (specifically a **prothrombin** (PT) or **activated** partial **thromboplastin time** (APTT) reagent) is added to a sample and formation of **fibrin** monitored over **time** by measuring some parameter that changes due to addition of reagent. The **rate** of change of this parameter, before **fibrin** is formed in the sample, is determined and if the **rate** exceeds a predetermined value, a second aliquot of sample is treated with (R) and the formation of precipitate monitored over **time**. In **method** (c), some parameter indicative of (P) is measured over **time**, the **rate** of change calculated and the process repeated at various **times**, with a change in the **rate** indicating progression or regression of the inflammatory state. The parameter is optical transmission or absorbance. In **method** (d), a sample is treated with (R) and some parameter that

changes due to formation of (P) is measured over **time** and its **rate** of change calculated. HD is diagnosed if the **rate** exceeds a predetermined level and appropriate treatment is administered, e.g. (i) antibiotic and/or CI or (ii) identification and correction of the underlying cause, e.g. administration of broad-spectrum antibiotic; evacuation of the uterus in abruptio placentae; **blood** replacement; administration of **platelet** concentrate (to correct **thrombocytopenia**), fresh **plasma**, **blood** factors and/or interleukin-1. The procedure may be repeated to optimize treatment. In **method** (e), a test sample is treated with a ligand (L) that can bind to CRP or (I), and this detected as part of a complex of proteins formed by adding a divalent metal **cation.** CRP may be intact, modified, cleaved or mutant. In **method** (f), a test sample is treated with (R) and kinetic or end-point measurements of precipitate formation made. A drug is then administered and the assay repeated, with an increase/decrease in precipitation indicating an effective drug.

ABEX UPTX: 20010502

EXAMPLE - The plot of transmission against **time** in a **standard activated** partial **thromboplastin time** (APTT) assay is **normally** sigmoid but in patients with disseminated intravascular **coagulation** (DIC) it is biphasic, with an initial region of low gradient and a subsequent region of steeper slope. The slope measured before start of **clot** formation is a significantly more specific and sensitive indicator of DIC than analysis of transmittance at a particular **time.** Particularly this slope was -0.001, or more negative, for all DIC patients and was -0.005 or more negative for 85 of 91 of them. **Normal** subjects, and those with abnormalities other than DIC, never had values more negative than -0.0002.

L62 ANSWER 13 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **2001-091718** [10] WPIX
CR 1997-052574 [05]; 1999-458146 [38]; 2000-514997 [46]; 2001-234924 [24]; 2002-147005 [19]
DNN **N2001-069462** DNC **C2001-027107**
TI Presentation of relationship between data comprises deriving at least one **time**-dependent measurement of the known **blood** samples, and computing **standard** deviation and determining the z-score for each derived predictor variable.
DC B04 S03
IN BECK, L; BRAUN, P; GIVENS, T B; GIVENS, T
PA (**ALKU**) **AKZO NOBEL NV**; (BECK-I) BECK L; (BRAU-I) BRAUN P; (GIVE-I) GIVENS T; (**INMR**) **BIOMERIEUX INC**
CYC 24
PI WO 2001001152 A1 20010104 (200110)* EN 36 G01N033-86 <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP KR US
AU 2000060676 A 20010131 (200124)
US 2002010553 A1 20020124 (200210) G06F019-00
EP 1188060 A1 20020320 (200227) EN G01N033-86 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
KR 2002042539 A 20020605 (200277) G01N033-86 <--
US 6502040 B2 20021231 (200305) G01N021-00
JP 2003529046 W 20030930 (200365) 28 G01N033-86 <--
AU 768436 B 20031211 (200404) G01N033-86 <--
ADT WO 2001001152 A1 WO 2000-US18310 20000630; AU 2000060676 A AU 2000-60676 20000630; US 2002010553 A1 CIP of US 1997-1647 19971231, US 1999-345080 19990630; EP 1188060 A1 EP 2000-947001 20000630, WO 2000-US18310 20000630; KR 2002042539 A KR 2001-716754 20011228; US 6502040 B2 CIP of US 1997-1647 19971231, US 1999-345080 19990630; JP 2003529046 W WO 2000-US18310 20000630, JP 2001-507105 20000630; AU 768436 B AU 2000-60676 20000630
FDT AU 2000060676 A Based on WO 2001001152; US 2002010553 A1 CIP of US 6321164; EP 1188060 A1 Based on WO 2001001152; JP 2003529046 W Based on WO

2001001152; AU 768436 B Previous Publ. AU 2000060676, Based on WO 2001001152

PRAI US 1999-345080 19990630; US 1997-1647 19971231

IC ICM G01N021-00; **G01N033-86**; G06F019-00

AB WO 200101152 A UPAB: 20040115

NOVELTY - Relationship between data is presented by providing data from each of the known **blood** samples; deriving at least one **time**-dependent measurement on the unknown **blood** sample; transforming data into predicator variable(s); computing **standard** deviation for each predictor variable; determining the z-score for each predictor variable.

DETAILED DESCRIPTION - Presentation of the relationship between data comprises:

(a) providing data from at least one **time** dependent measurement profile for each of the known **blood** samples;

(b) measuring a respective property over **time** to derive at least one **time**-dependent measurement on the unknown **blood** sample;

(c) transforming data from (a) and (b) to predicator variable(s) which captures the content of both the unknown and known **blood** sample's **time**-dependent measurement profiles;

(d) computing **standard** deviation for each variable in (c) of the known sample of (a); and

(e) determining the z-score for each predictor variable, and determining if z-score(s) for the unknown sample is greater than a predetermined limit, signifying that the unknown sample is different from the known population represented by the **model.**

USE - The **method** is for presenting the relationship between data from an assay relating to **thrombosis**-hemostasis on an unknown sample, and data from assays relating **thrombosis** -hemostasis from known populations.

ADVANTAGE - The **method** facilitates analysis of information embedded in the data from **coagulation** assays that is not included in the conventional analysis. The additional information discriminates between underlying conditions and aid in the identification of undetected conditions.

DESCRIPTION OF DRAWING(S) - The figure is a diagram illustrating the key aspect of the invention.

Dwg.7/7

FS CPI EPI

FA AB; GI; DCN

MC CPI: B04-C02E1; **B04-H19**; B11-C08E; **B12-K04A2**

EPI: **S03-E14H**

TECH UPTX: 20010220

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred **Method** : The data in (c) is transformed into predicator variable(s) that includes timing, **rate** and/or magnitude of changes during the **time** -dependent profile. **Coagulation** assays are performed in (a) and (b) to provide profiles. The unknown sample is removed by an automated probe from the sample container to a test well. Reagent(s) are added to the test well to **initiate** property changes within the sample. The development of the property over **time** is monitored to derive the optical data profile. The z-scores is stored in memory of the analyzer and/or displayed on the analyzer. Maps are provided for presenting the data.

Preferred Variable: The predictor variable in (c) includes a minimum(s) of the two derivative of the profile; **time** index(es) on the minimum of two derivatives; maximum(s) and **time** index(es) of the second derivative; overall change(s) in the **coagulation** parameter during the **time**-dependent measurement on the unknown sample; **clotting time**(s); and slope(s) of the profile before and after **clot** formation.

Preferred Sample: The known **blood** samples are whole

blood or **plasma** from which information is known relating to intrinsic or extrinsic(s) **clotting** factors and/or therapeutic agents or are **normal** samples.
Preferred Profile: The **time**-dependent measurement profile(s) comprise(s) profile from PT, APTT, preferably optical measurements made from multiple wavelengths that correspond to light scattering changes or light absorption in the sample. At least one optical profile is provided with an automated analyzer for **thrombosis** and hemostasis testing.

L62 ANSWER 14 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-024512 [03] WPIX
DNN N2001-019191 DNC C2001-007324
TI Detection of **coagulation** abnormalities, e.g., those associated with autoimmune disorders, by **comparison** of **thrombin** generation **rates** achieved using defibrinated **plasma** samples.
DC B04 S03
IN KRILIS, S
PA (SESY-N) SOUTHEASTERN SYDNEY AREA HEALTH SERVICE
CYC 93
PI WO 2000062077 A1 20001019 (200103)* EN 24 G01N033-86 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000036486 A 20001114 (200108)
EP 1173771 A1 20020123 (200214) EN G01N033-86 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2002541484 W 20021203 (200309) 28 G01N033-86 <--
AU 768038 B 20031127 (200404) G01N033-86 <--
ADT WO 2000062077 A1 WO 2000-AU309 20000412; AU 2000036486 A AU 2000-36486 20000412; EP 1173771 A1 EP 2000-915041 20000412, WO 2000-AU309 20000412; JP 2002541484 W JP 2000-611088 20000412, WO 2000-AU309 20000412; AU 768038 B AU 2000-36486 20000412
FDT AU 2000036486 A Based on WO 2000062077; EP 1173771 A1 Based on WO 2000062077; JP 2002541484 W Based on WO 2000062077; AU 768038 B Previous Publ. AU 2000036486, Based on WO 2000062077
PRAI AU 1999-9712 19990412
IC ICM **G01N033-86**
ICS **C12Q001-56**; **G01N033-49**
AB WO 200062077 A UPAB: 20010116
NOVELTY - A **comparison** of **thrombin** generation **rates** achieved by reaction of an **activator** of **thrombin** with defibrinated **normal** **plasma**, in the presence and absence of a defibrinated test **plasma** sample, is used to detect **coagulation** abnormalities in the test **plasma** sample.
DETAILED DESCRIPTION - Detection of **coagulation** abnormalities in a **plasma** sample comprises:
(a) determining a test **rate** of **thrombin** generation over a given **time** interval by reacting an **activator** of **thrombin** with defibrinated **normal** **plasma** (DNP) in the presence of a defibrinated test **plasma** sample;
(b) determining a control **rate** of **thrombin** generation over the same **time** interval as in (a) by reacting an **activator** of **thrombin** with DNP in the absence of any defibrinated test **plasma**; and
(c) **comparing** the **rates** of **thrombin**

generation in steps (a) and (b). Any significant difference between the two **thrombin** generation **rates** is indicative of a **coagulation** abnormality in the test **plasma**.

USE - The process is useful for detecting **clotting** abnormalities in **plasma** samples. It may be used to detect decreased **clotting** potential, which can occur as a result of sepsis, severe trauma or autoimmune conditions. It may be used to detect increased **clotting** potential, which can occur with lupus, other autoimmune conditions or the presence of autoantibodies to beta 2-GPI, **prothrombin** or other antigens that induce **antiphospholipid** antibodies to occur. It can be used to identify patients at risk of clinical **thrombotic** events.

ADVANTAGE - The process is simple to carry out, and can identify both anticardiolipin and lupus **anticoagulant** type antibodies. It can discriminate between infective and autoimmune type anticardiolipin autoantibodies.

Dwg.0/9

FS CPI EPI

FA AB; DCN

MC CPI: **B04-B04D4**; **B04-H19**; B11-C08; B11-C08A; B12-K04E
EPI: **S03-E14H**

TECH UPTX: 20010116

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Process: The **activator** of **thrombin** is **thromboplastin**, kaolin, Russell Viper venom or silica, especially **thromboplastin** . The **time** interval is 20 minutes. The **thrombin** generation is measured by adding a substrate which is converted by the generated **thrombin** to a detectable product. This substrate is especially spectrozyme. **Thrombin** formation in (a) and (b) is measured in optical density units, and the units obtained are placed on the Y axis and plotted over **time** (in minutes) on an X axis to give a sigmoidal curve. A shift in the curve to the left indicates accelerated **thrombin** generation, and a shift to the right indicates inhibition of **thrombin** formation in the test **plasma** sample. Changes may be quantified by expressing the results as a **ratio** of the **normal** curve using the mean of three data points on a linear portion of the curve.

ABEX UPTX: 20010116

EXAMPLE - A typical process used ELISA 96 well plates to which **thromboplastin** (diluted 1/10 in 0.9% NaCl; 25 microl), test antibody (diluted in 0.9% NaCl; final concentration 6.25 microg/ml; 25 microl) and pooled defibrinated **plasma** (1/4 dilution in 0.9% NaCl; 50 microl) were added. The mixture was incubated at 37degreesC for 10 minutes. Spectrozyme (diluted 1/5 in 0.9% NaCl; 50 microl) was added at room temperature, followed by CaCl (30 mM in 0.9% NaCl; 50 microl) at room temperature. The **time** started on the addition of CaCl. The absorbance was read at 405 nm every 2 minutes. A typical curve was a skewed S shape, and the readings were stopped when a plateau was reached at an optical density of 1.2.

L62 ANSWER 15 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2000-663458 [64] WPIX

DNN N2000-491495 DNC C2000-200997

TI **Method** for diagnosing hemostasis system disorder in circulatory shock patients.

DC B04 S03

IN KNYSH, A S; SHIPAKOV, V E; SHPISMAN, M N; TYUTRIN, I I

PA (KNYS-I) KNYSH A S; (SHIP-I) SHIPAKOV V E; (SHPI-I) SHPISMAN M N; (TYUT-I) TYUTRIN I I; (UYSI-R) UNIV SIBE MED

CYC 1

PI RU 2151401 C1 20000620 (200064)* G01N033-86 <--

ADT RU 2151401 C1 RU 1998-114538 19980716

PRAI RU 1998-114538 19980716

IC ICM **G01N033-86**
ICS **G01N033-49**
AB RU 2151401 C UPAB: 20001209
NOVELTY - **Method** involves determining response period, spontaneous **blood platelets** aggregation intensity, **prothrombin** constant, maximum amplitude, **clot fibrin-blood-platelet** structure formation **time**, general retraction and spontaneous **clot** lysis index. Response period being found to be within 5-7 min, spontaneous **blood platelets** aggregation intensity being from -2 to -6 relative units, **prothrombin** constant being equal to 4-6 min, maximum amplitude being within the limits of 500-700 relative units, **clot fibrin-blood- platelet** structure formation **time** being within the limits of 40-60 min, general retraction and spontaneous **clot** lysis index being equal to 10- 20%, no shock case is to be diagnosed. Spontaneous **blood platelets** aggregation intensity being from -8 to -14 relative units and no changes in the other values being observed, compensated shock stage is to be diagnosed. Response period being found to be less than 4 min, spontaneous **blood platelets** aggregation intensity being from -8 to -14 relative units, **prothrombin** constant being less than 3 min, maximum amplitude being greater than 750 relative units, **clot fibrin-blood-platelet** structure formation **time** being less than 40 min, general retraction and spontaneous **clot** lysis index being equal to 10-20%, decompensated reversible shock stage is to be diagnosed. Response period being found to be greater than 10 min, spontaneous **blood platelets** aggregation intensity being equal to -4 relative units, **prothrombin** constant being greater than 9 min, maximum amplitude being less than 400 relative units, **clot fibrin-blood-platelet** structure formation **time** being greater than 70 min, general retraction and spontaneous **clot** lysis index being greater than 20% or less than 5%, decompensated irreversible shock stage is to be diagnosed.
USE - Medicine.
ADVANTAGE - Enhanced accuracy of the **method**; accelerated **method**. 1 dwg
Dwg.0/0
FS CPI EPI
FA AB
MC CPI: **B04-B04D5**; B11-C08E; B12-K04A
EPI: **S03-E14H**; **S03-E14H1**

L62 ANSWER 16 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **2000-514997** [46] WPIX
CR 1997-052574 [05]; 1999-458146 [38]; 2001-091718 [10]; 2001-234924 [24]; 2002-147005 [19]
DNN **N2000-380594** DNC **C2000-153705**
TI Predicting **hemostatic** dysfunction by measuring property of **blood** sample over **time** and creating **time**-dependent measurement profile.
DC B04 P31 S03
IN DOWNEY, C; **FISCHER, T J**; TOH, C H
PA (**ALKU**) **AKZO NOBEL NV**
CYC 24
PI WO 2000046603 A1 20000810 (200046)* EN 111 G01N033-86 <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP KR US
AU 2000034833 A 20000825 (200059)
EP 1147423 A1 20011024 (200171) EN G01N033-86 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002541431 W 20021203 (200309) 105 G01N033-86 <--
ADT WO 2000046603 A1 WO 2000-US2987 20000204; AU 2000034833 A AU 2000-34833

20000204; EP 1147423 A1 EP 2000-913371 20000204, WO 2000-US2987 20000204; JP 2002541431 W JP 2000-597634 20000204, WO 2000-US2987 20000204
FDT AU 2000034833 A Based on WO 2000046603; EP 1147423 A1 Based on WO 2000046603; JP 2002541431 W Based on WO 2000046603
PRAI US 1999-244340 19990204
IC ICM **G01N033-86**
ICS **A61B005-145**
AB WO 200046603 A UPAB: 20030603
NOVELTY - Predicting **hemostatic** dysfunction comprises defining predictor variables (110), e.g. the slope of a **time**-dependent profile. A **model** is derived (113) that represents the relationship between the dysfunction and the variables from known samples (115). The **model** is used to predict the existence of **hemostatic** dysfunction.
USE - The predicted **hemostatic** dysfunction is especially disseminated intravascular **coagulation.**
ADVANTAGE - The prediction can be made from a **time** -dependent measurement profile without artificial manipulation of samples.
DESCRIPTION OF DRAWING(S) - The figure is a chart illustrating the steps of the process.
Definition of predictor variables 110
Derivation of **model** 113
Predictor variables from known samples 115
Dwg.31/45
FS CPI EPI GMPI
FA AB; GI
MC CPI: B11-C08E; **B12-K04A2**
EPI: **S03-E14H**
TECH UPTX: 20000921
TECHNOLOGY FOCUS - BIOLOGY - Preferred **method**: The **time** -dependent measurement is an optical profile provided by an automated analyzer for **thrombosis** and **hemostatic** testing. A number of optical measurements are taken at one or more wavelengths to derive the optical profile, the measurements corresponding to changes in light transmission through the sample. Results of predicted congenital or acquired imbalance or therapeutic condition are automatically stored in a memory of an automated analyzer and/or displayed. Assays for confirming the existence of the condition are automatically performed. The **time**-dependent measurement profiles are derived from assays **initiated** with PT, APTT, fibrinogen or TT reagents. Additional patient medical data e.g. fibrinogen, D-dimer or **platelet** count information, may also be used for predicting the condition. The dysfunction prediction may be performed a number of **times** to monitor disease progression or regression in the patient.

L62 ANSWER 17 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **2000-412008** [35] WPIX
DNN **N2000-307978** DNC **C2000-124866**
TI Performance of **blood coagulation** assays with **clotting** monitored by piezoelectric sensing.
DC A96 B04 S03
IN MORENO, M; WU, J R
PA **(ALKU) AKZO NOBEL NV**
CYC 24
PI WO 2000031529 A1 20000602 (200035)* EN 40 G01N033-00 <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP KR US
AU 2000017331 A 20000613 (200043) G01N033-00 <--
US 6200532 B1 20010313 (200120) G01N033-00 <--
EP 1141699 A1 20011010 (200167) EN G01N033-00 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 2000031529 A1 WO 1999-US27287 19991117; AU 2000017331 A AU 2000-17331 19991117; US 6200532 B1 US 1998-197481 19981120; EP 1141699 A1 EP

1999-960444 19991117, WO 1999-US27287 19991117
FDT AU 2000017331 A Based on WO 2000031529; EP 1141699 A1 Based on WO 2000031529
PRAI US 1998-197481 19981120
IC ICM **G01N033-00**
AB WO 200031529 A UPAB: 20000725
NOVELTY - A reaction chamber (1) in a housing has a **blood** sample inlet. A generator (6) passes electromagnetic waves through the sample in the reaction chamber. A piezoelectric device (3) monitors changes to the waves after passing through the sample to detect a changing **coagulation** parameter of the sample.

DETAILED DESCRIPTION - Mechanical vibration is created using a bender (2) made of a thin iron film attached to the piezoelectric film (3). Variations in the bender movement are detected by the piezoelectric device that provides a signal corresponding to the **time** required for the formation of a **fibrin clot.** An electric circuit (7) collects the signal generated by the piezoelectric device. A differential amplifier enhances the signal. A separation membrane may be used to separate red **blood** cells from whole **blood** in the event that a **plasma** sample is desired. The membrane may be provided as part of the point-of-care device. A mechanism may be provided to compensate for the effect of the different hematocrit content in a patient's whole **blood** sample in a device for measuring one or more **coagulation** parameter.

USE - The device performs **blood coagulation** assays, particularly **prothrombin times**, **activated** partial **thromboplastin times** and other **clotting** tests.

ADVANTAGE - It is easy to use, accurate and rapid for routine testing at a patient's bedside, physician's office, operating room, or patient's home for patients undergoing **anticoagulant** therapy.

DESCRIPTION OF DRAWING(S) - The figure shows a cross-sectional view through the test device.

reaction chamber 1
magnetic bender 2
piezoelectric film 3
electromagnetic wave generator 6
electric circuit 7

Dwg.2/14
FS CPI EPI
FA AB; GI; DCN
MC CPI: A12-V03B; **B04-B04D5**; **B04-H19**; B11-C08B; **B12-K04A2**
EPI: S03-E02X; S03-E12; **S03-E14H1**

L62 ANSWER 18 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-561378 [47] WPIX
DNN N1999-414814 DNC C1999-163562
TI Analytical **method** for qualitative and optionally quantitative determination of **polymerization** and/or **coagulation** in fluids containing **polymerizable** and/or **coagulable** components.
DC A35 B04 D14 D16 J04 S03
IN LUNDSTROEM, I; TENGVALL, P; LUNDSTROM, I
PA (GLOB-N) GLOBAL HEMOSTASIS INST MGR AB
CYC 85
PI WO 9944060 A1 19990902 (199947)* EN 24 G01N033-49 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW

AU 9930296 A 19990915 (200004) G01N033-49 <--
EP 1058848 A1 20001213 (200066) EN G01N033-49 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002505429 W 20020219 (200216) 27 G01N021-27
US 6379976 B1 20020430 (200235) G01N033-53 <--
EP 1058848 B1 20020918 (200269) EN G01N033-49 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
DE 69903002 E 20021024 (200278) G01N033-49 <--

ADT WO 9944060 A1 WO 1999-EP1156 19990223; AU 9930296 A AU 1999-30296 19990223; EP 1058848 A1 EP 1999-911696 19990223, WO 1999-EP1156 19990223; JP 2002505429 W WO 1999-EP1156 19990223, JP 2000-533757 19990223; US 6379976 B1 WO 1999-EP1156 19990223, US 2000-622063 20001114; EP 1058848 B1 EP 1999-911696 19990223, WO 1999-EP1156 19990223; DE 69903002 E DE 1999-603002 19990223, EP 1999-911696 19990223, WO 1999-EP1156 19990223

FDT AU 9930296 A Based on WO 9944060; EP 1058848 A1 Based on WO 9944060; JP 2002505429 W Based on WO 9944060; US 6379976 B1 Based on WO 9944060; EP 1058848 B1 Based on WO 9944060; DE 69903002 E Based on EP 1058848, Based on WO 9944060

PRAI SE 1998-590 19980226

IC ICM G01N021-27; **G01N033-49**; **G01N033-53**
ICS G01J003-45; **G01N033-00**; **G01N033-48**; **G01N033-543**; **G01N033-86**

AB WO 9944060 A UPAB: 19991116
NOVELTY - Analytical **method** for qualitative and optionally quantitative determination of **polymerization** or **coagulation** in fluids containing **polymerizable** or **coagulable** components involves measuring changes in reflected beams of incident beams of electromagnetic radiation.

DETAILED DESCRIPTION - Analytical **method** of qualitative and optionally quantitative determination of **polymerisation** or **coagulation** comprises:

(a) **initiating polymerization** or **coagulation** in fluid;

(b) contacting fluid or sample with a film of electrically conducting material on a support that is transparent for electromagnetic radiation used and is more optically dense than the fluid;

(c) directing incident beams of electromagnetic radiation through the support, to the back of the film, at angles equal to or greater than the critical angle for total reflection;

(d) measuring changes in the reflected beams due to changes in the surface plasmon resonance angle;

(e) repeating (c) and (d) at least once;

(f) registering the occurrence and magnitude of changes measured in (d) and

(g) correlating the occurrence and magnitude of changes with qualitative and optionally quantitative occurrence of **polymerization** or **coagulation** in the fluid.

USE - Used for qualitative and optionally quantitative determination of **polymerization** or **coagulation** in fluids containing **polymerizable** or **coagulable** components (claimed) including biological fluids, such as **blood** or **blood plasma** (claimed) and milk, lymph, sperm, and synovial fluid, and **polymerization** reaction fluids, including paints, lacquers, glues, thermosetting plastics, thermoplastics, acrylamides, agarose and foodstuffs including sauce, custard, mousse, jelly or sugar (claimed).

The **method** is also used to determine presence of **initiators** such as **thromboplastin**.

A drop of whole **blood** (50 mu l), obtained by skin puncture of a fingertip of an apparently healthy volunteer, was transferred with a plastic pipette tip onto a 45 nm gold film covered with dry immobilized thermoplastin, a **coagulation** inhibitor. The gold film was supported on a glass slide, which was placed on the flat side of the semi-spherical rod prism of a modified BIAlite (RTM) surface plasmon

resonance instrument. The prism and slide with the god film were temperature equilibrated at 22 deg. C. An instrument run, with continuous registrations of shift in surface plasmon resonance angle, was started some minutes prior to applying the drop of **blood.**

The sensogram produced was interpreted as follows. Application of the drop of **blood** on the gold film resulted in large changes in instrument readout at 180 seconds. The readout then stabilized at 33500 RU. At 240 seconds, the readout began to increase and increased continuously for some minutes, reaching a plateau of 35500 RU at 400 seconds. In total, during the **time** period 240-400 seconds, the readout increased by 2000 RU. This relatively large increase, a relatively large signal, was caused by **coagulation** of the **blood** and was related to the magnitude of **coagulation.** In separate experiments, the **coagulation** was confirmed by touching the drop of blood on the gold film with the tip of a plastic pipette. At 240 seconds, the drop of **blood** was liquid, but at 400 seconds, the drop of **blood** was **coagulated**, i.e. transformed into a gel. The results demonstrate that the occurrence of **coagulation** in whole **blood, initiated** by **thromboplastin**, was readily qualitatively and optionally quantitatively determined by the analytical **method.**

ADVANTAGE - The **method** places no, or small, requirements on fluid volume, thus fluid volume size and precision in fluid transfer is not of importance for analytical results. The **method** allows determinations in severe-condition situations e.g. inside high-pressure and -temperature **polymerization** reactors, such as in the production of polyethylene, and on-line determinations inside flow through industrial reactors and the circulatory system.

DESCRIPTION OF DRAWING(S) - Sensogram of **coagulation** in a drop of whole **blood initiated** by immobilized **thromboplastin.** Instrument response (shift in surface plasmon resonance angle) expressed in resonance units (RU) is plotted against **time.**

Dwg.1/3

FS CPI EPI

FA AB; GI; DCN

MC CPI: A09-B; A10-B01; A10-C01; A10-D; **B04-B04D5**; B04-C03B; B05-A01B; B05-A03B; B05-B02C; B11-C01; B11-C08; B12-K04; D03-K03; D03-K04; **D05-H09**; J04-C

EPI: **S03-E14H**; **S03-E14H1**

TECH UPTX: 19991116

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred **method** : (a), (b) and (c) are effected simultaneously or in an alternative order. (e) is effected continuously. **Initiation** of **polymerization** or **coagulation** is spontaneous is effected by changes of one or several conditions within the fluid chosen from temperature, pressure, ionic strength, pH and/or redox potential, or is effected by at least one **initiator**, preferably attached to the surface of the film in contact with the fluid.

Changes in the reflected beams due to changes in the surface plasmon resonance angle are polarization changes in relation to the polarization of incident beams or incident changes. The wavelength of incident light is chosen to coincide with the absorption wavelength(s) of the fluid.

Preferred films: The film of electrically conducting material is comprising at least one of gold, silver, platinum, aluminum or electrically conducting **polymer.** The thickness of the film is 10-1000 nm.

Preferred film support: The film support comprises glass or plastic and is in the form of a plate, half sphere, half-spherical rod, optical fiber, beaker, cuvette, test tube or reactor window.

TECHNOLOGY FOCUS - BIOLOGY - The fluid is a biological fluid, preferably **blood** or **blood plasma**, more preferably mixed

with at least one **coagulation** inhibitor, especially heparin, hirudin, anti-**thrombin**, **tissue factor** **pathway** inhibitor, C1-inhibitor and/or Ca2+ activity lowering agent and/or at least one **coagulation initiator**, especially negatively charged surfaces including silica and ellergic acid derivatives, **phospholipids**, **thromboplastin**, endothelial cells and cell membranes, **thrombocytes** and their cell membranes, monocytes and their cell membranes or any required **coagulation** factor lacking from the fluid.

TECHNOLOGY FOCUS - **POLYMERS** - The fluid is a **polymerization** reaction fluid, preferably a paint, lacquer, glue, thermosetting plastic, thermoplastic, acrylamide, agarose, foodstuff including sauce, custard, mousse, jelly or sugar.

L62 ANSWER 19 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **1999-458146** [38] WPIX
CR 1997-052574 [05]; 2000-514997 [46]; 2001-091718 [10]; 2001-234924 [24]; 2002-147005 [19]
DNN **N1999-342695** DNC **C1999-134481**
TI Predicting presence of abnormal levels of protein in **blood** **clotting** cascade.
DC B04 S03 T01
IN BRAUN, P; **FISCHER, T J**; GIVENS, T B
PA (**ALKU**) **AKZO NOBEL NV**; (BRAU-I) BRAUN P; (FISC-I) FISCHER T J; (GIVE-I) GIVENS T B; (**INMR**) **BIOMERIEUX SA**
CYC 24
PI WO 9934208 A1 19990708 (199938)* EN 94 G01N033-49 <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP KR US
AU 9919503 A 19990719 (199951)
EP 1042669 A1 20001011 (200052) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
KR 2001033817 A 20010425 (200164) G01N033-49 <--
US 6321164 B1 20011120 (200174) G01N021-00
JP 2002500360 W 20020108 (200206) 82 G01N033-68 <--
US 2002019706 A1 20020214 (200214) G06F019-00
US 6564153 B2 20030513 (200335) G01N021-00
ADT WO 9934208 A1 WO 1998-US27865 19981230; AU 9919503 A AU 1999-19503 19981230; EP 1042669 A1 EP 1998-964342 19981230, WO 1998-US27865 19981230; KR 2001033817 A KR 2000-707373 20000630; US 6321164 B1 Cont of US 1995-477839 19950607, CIP of US 1997-859773 19970521, US 1997-1647 19971231; JP 2002500360 W WO 1998-US27865 19981230, JP 2000-526808 19981230; US 2002019706 A1 Cont of US 1995-477839 19950607, CIP of US 1997-859773 19970521, Cont of US 1997-1647 19971231, US 2001-850255 20010507; US 6564153 B2 Cont of US 1995-477839 19950607, CIP of US 1997-859773 19970521, Cont of US 1997-1647 19971231, US 2001-850255 20010507
FDT AU 9919503 A Based on WO 9934208; EP 1042669 A1 Based on WO 9934208; US 6321164 B1 Cont of US 5708591, CIP of US 6101449; JP 2002500360 W Based on WO 9934208; US 2002019706 A1 Cont of US 5708591, CIP of US 6101449, Cont of US 6321164; US 6564153 B2 Cont of US 5708591, CIP of US 6101449, Cont of US 6321164
PRAI US 1997-1647 19971231; US 1995-477839 19950607;
US 1997-859773 19970521; US 2001-850255 20010507
IC ICM G01N021-00; **G01N033-49**; **G01N033-68**; G06F019-00
ICS G01N031-00; **G01N033-86**
AB WO 9934208 A UPAB: 20030603
NOVELTY - Predicting the presence of an abnormal level of at least 1 protein in the **clotting** cascade from at least one **time** -dependent measurement profile involves using a **model** that represents the relationship between the abnormal level of the protein in the **clotting** cascade and a set of predictor variables.

DETAILED DESCRIPTION - Predicting the presence of an abnormal level of at least 1 protein in the **clotting** cascade from at least one **time**-dependent measurement profile comprises:

(1) performing at least one **time**-dependent measurement on an unknown sample and measuring a respective property over **time** to derive a **time**-dependent measurement profile;

(2) defining a set of predictor variables which define the data of the **time**-dependent measurement profile;

(3) deriving a **model** that represents the relationship between the abnormal level of the protein in the **clotting** cascade and the set of predictor variables and

(4) using the **model** of step (c) to predict the existence of the abnormal level of the protein in the **clotting** cascade and to predict which protein or proteins in the **clotting** cascade are at an abnormal level.

The prediction of the protein or proteins at an abnormal level is a better prediction than an abnormal **clot time** alone.

An INDEPENDENT CLAIM is also included for presenting a relationship between data from an assay relating to **thrombosis**-hemostasis on an unknown sample and data from assays relating to **thrombosis** -hemostasis from known sample populations which comprises:

(A) providing data from at least one **time** dependent measurement profile for each of known **blood** samples;

(B) performing at least one **time**-dependent measurement on an unknown **blood** sample and measuring a respective property over **time** to derive at least one **time**-dependent measurement profile for the unknown **blood** sample;

(C) transforming data from step (2) to predictor variables which capture the information content of both the unknown **blood** sample **time**-dependent measurement profile and the known **blood** sample **time**-dependent measurement profiles and

(D) presenting the data from the unknown **blood** sample **time**-dependent measurement profile relative to the data from the known **blood** sample **time**-dependent measurement profiles.

USE - Used for estimating the concentration of at least one protein in the **clotting** cascade.

Dwg.0/30

FS CPI EPI

FA AB; DCN

MC CPI: **B04-B04D2**; B04-N04; B11-C07; B12-K04

EPI: **S03-E14H**; **S03-E14H1**; T01-J

TECH UPTX: 19990922

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **method**: In the prediction of the protein at an abnormal level, the specificity is at least 0.85 and the sensitivity is greater than 0.6. The samples with a measured concentration of less than 30% of **normal** for a specific factor are defined as being at an abnormal level.

The **time**-dependent measurement profile is at least one optical profile is produced by an automated analyzer for **thrombosis** and hemostasis testing. A number of optical measurements at one or more wavelengths are taken over **time** to derive at least one optical profile. The optical measurements correspond to changes in light scattering and/or light absorption in the unknown sample. The optical measurements are taken over **time** to derive at least one optical profile, and the optical measurements are each **normalized** to a first optical measurement. At least one optical profile is produced automatically by an analyzer. The unknown sample is automatically removed by an automated probe from a sample container to a test well. One or more reagents are automatically added to the test well to **initiate** the property changes within the sample. The development of the property over **time** is automatically optically monitored.

A predicted congenital or acquired imbalance or therapeutic condition is

automatically stored in a memory of the automated analyzer and/or displayed on the automated analyzer. Assays for confirming the existence of the congenital or acquired imbalance or therapeutic condition are automatically effected. A set of data from known samples is produced which is used for deriving the **model.** The data from known samples is obtained by performing assays on the known samples.

Time dependent measurement profiles include at least two profiles from assays **initiated** with PT reagents, APTT reagents, fibrinogen reagents and TT reagents.

In (1), steps (3) and (4) comprise transforming a set of input parameters from the **time**-dependent measurement profiles for the known **blood** samples and the unknown **blood** sample, to corresponding individual output neurons whose location on an output map corresponds to the respective input data. Step (4) also comprises:

(1) selecting weight vectors;

(2) selecting a sample from a training set;

(3) identifying best matching winning neuron at a particular **time** ;

(4) updating weight vectors and

(5) repeating steps (1)-(4) until the map reaches equilibrium.

In step (3), data from the **time**-dependent measurement profiles is transformed into predictor variables that characterize timing, **rate** and magnitude of changes during the **time**-dependent measurement profile and the predictor variables are used as input for neural networks. The definition of the predictor variables is a position in a self-organizing feature map, trained with data from the **time** -dependent measurement profiles for the known **blood** samples.

Preferred materials: The proteins comprise factors II, V, VII, VIII, IX, X, XI and/or XII. The known **blood** samples and the unknown **blood** sample are samples of whole **blood**, **plasma** , or other part of whole **blood.** The known **blood** samples are samples of which are information is known relating to one or more intrinsic or extrinsic **clotting** factors and/or therapeutic agents. The known **blood** samples are samples of which are known the presence or absence of one or more abnormalities relating to at least one of fibrinogen level, oral **anticoagulant**, heparin, and one or more factor levels.

In step (4) one or more of **normal** sample, presence of heparin, and one or more factor deficiencies are presented on a PT map, or at least one of **normal** specimen, presence of heparin, abnormal fibrinogen, oral **anticoagulant**, and one or more factor deficiencies are presented on an APTT map. The predictor variables are in terms of a **standard** deviation from a mean of at least one known **blood** sample population, and the unknown **blood** sample is characterized by variation from the mean of the known **blood** samples for each predictor variable.

ABEX UPTX: 19990922

EXAMPLE - No relevant example given.

L62 ANSWER 20 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-373178 [32] WPIX
DNN N1999-278551 DNC C1999-110250
TI Detecting **haemostasis** defects, using **clotting** agent and/or **anticoagulating** agent.
DC B04 D16 S03
IN KRAUS, M; SCHELP, C; WIEGAND, A
PA (DADE-N) DADE BEHRING MARBURG GMBH
CYC 29
PI EP 924523 A2 19990623 (199932)* GE 17 G01N033-86 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
DE 19756773 A1 19990624 (199932) G01N033-50 <--
AU 9897182 A 19990708 (199938) G01N033-50 <--

JP 11242035	A	19990907 (199947)		13	G01N033-86	<--
CA 2256089	A1	19990619 (199949)	EN		C12Q001-56	<--
US 6187594	B1	20010213 (200111)			G01N033-86	<--
US 6482653	B1	20021119 (200280)			G01N033-86	<--
US 2003027235	A1	20030206 (200313)			C12Q001-56	<--
US 6750032	B2	20040615 (200439)			C12Q001-52	<--

ADT EP 924523 A2 EP 1998-122888 19981202; DE 19756773 A1 DE 1997-1056773 19971219; AU 9897182 A AU 1998-97182 19981217; JP 11242035 A JP 1998-360662 19981218; CA 2256089 A1 CA 1998-2256089 19981215; US 6187594 B1 US 1998-215167 19981218; US 6482653 B1 Cont of US 1998-215167 19981218, US 2000-604271 20000626; US 2003027235 A1 Cont of US 1998-215167 19981218, Div ex US 2000-604271 20000626, US 2002-255632 20020927; US 6750032 B2 Cont of US 1998-215167 19981218, Div ex US 2000-604271 20000626, US 2002-255632 20020927

FDT US 6482653 B1 Cont of US 6187594; US 2003027235 A1 Cont of US 6187594, Div ex US 6482653; US 6750032 B2 Cont of US 6187594, Div ex US 6482653

PRAI DE 1997-19756773 19971219

IC ICM **C12Q001-52**; **C12Q001-56**; **G01N033-50**; **G01N033-86**

ICS G01N021-75; G01N021-76; G01N021-77; **G01N033-546**

AB EP 924523 A UPAB: 19991122

NOVELTY - Detecting **haemostasis** defects comprises adding a **clotting** agent and/or an **anticoagulating** agent at **time** intervals which causes or inhibits an energy transfer between the agents, which can be measured.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a diagnostic composition comprising the **blood clotting** substances and **anticoagulating** substances used in the **method** above.

USE - The **method** can be used to detect genetic and/or acquired lack of **blood clotting** factors or factors of the fibrinolytic system, genetic defects of **thrombocytes**, disease-associated or disease therapy-associated **haemostasis** defects and/or genetic and/or acquired defects of the complement system. The **method** can be used to establish the lack of certain factors necessary for **blood clot** formation, and for testing the aggregation ability of **platelets** (all claimed).

Dwg.0/3

FS CPI EPI

FA AB; DCN

MC CPI: B04-B01B; B04-C02C; B04-C03; B04-N04; B05-B01B; B05-B02C; B05-U02; B06-A03; B06-D18; B06-F02; B10-F02; B11-C07B3; B11-C08E3; B12-K04A; **D05-H09**

EPI: **S03-E14H**

TECH UPTX: 19990813

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred materials: The energy transfer is caused by short-lived molecules such as singlet oxygen, radiation with low intensity, e.g. radioactive beta-radiation and/or energy transfer according to Foerster. The activity of the agents can be enhanced or inhibited by other substances, which will change the measurable signal strength by changing the polarity and intensity of the light, inhibiting or enhancing of enzyme activity and/or changing fluorescence. The agents are capable to bind to the **blood clot** via direct or indirect non-specific hydrophobic or electrostatic exchange. The agents are bound to or are encased in suspendable particles via covalent binding, specific binding and adsorption. The particles are selected from colored crystals, alloys, silicas, magnet particles, oil droplets, lipid particles, dextran, protein aggregates and, especially latex particles. The particles can be further treated after their initial preparation and can comprise adsorptively or covalently bound coating layers or shells, comprising proteins, carbohydrates, lipophilic substances, bio-**polymers** and/or organic **polymers**. The **method** also measures the

blood clotting time, partial
thromboblast time, **thromboblast time**
, **protein C activation time**,
Russel viper venom **time** and **thrombin time.**
The diagnostic substances used in the **method** also comprises
factors of the **blood clotting** reaction.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Agent: The agents are selected from photosensitising and chemiluminescent compounds which can be **activated** to generate singlet oxygen and light radiation, respectively. The photosensitising compounds are acetone, benzophenone, 9-thioxanthone, eosin, 9,10-dibromoanthrazene, chlorophyll, buckminsterfullerene, methylene blue, rose Bengal, porphyrines, phthalocyanine and/or their derivatives. The chemiluminescent compounds are selected from olefins, 9-alkylidenexanthane, 9-alkylidene-N-alkylacridane, enolether, enamine, arylvinylether, dioxene, arylimidazone and/or lucigenin. The chemiluminescent compounds are brought into contact with fluorophores to enhance emission of light of higher wavelength. Fluorescent compounds, e.g. 1,3-di-phenylisobenzofuran, which react with singlet oxygen by photobleaching, or, e.g. oxenumbelliferylether, which react with singlet oxygen to form fluorophore precursors.

ABEX UPTX: 19990813
EXAMPLE - None given.

L62 ANSWER 21 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-359879 [31] WPIX
DNC C1999-106698
TI Determination of **antithrombin** III in **plasma** sample, useful for diagnosing patients at risk of **thrombosis.**
DC B04 D16
IN TRISCOTT, M X
PA (SIGM-N) SIGMA-ALDRICH CO; (TRIN-N) TRINITY BIOTECH MFG LTD
CYC 29
PI EP 927767 A2 19990707 (199931)* EN 24 C12Q001-56 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
AU 9895156 A 19990701 (199937) C12Q001-56 <--
JP 11235197 A 19990831 (199946) 19 C12Q001-56 <--
CA 2255255 A1 19990609 (199948) EN C12Q001-56 <--
US 5985582 A 19991116 (200001) G01N033-86 <--
AU 730231 B 20010301 (200117) C12Q001-56 <--
AU 2000072346 A 20010329 (200124)# G01N033-96 <--
AU 744025 B 20020214 (200223)# G01N033-96 <--
ADT EP 927767 A2 EP 1998-310023 19981208; AU 9895156 A AU 1998-95156 19981202; JP 11235197 A JP 1998-349902 19981209; CA 2255255 A1 CA 1998-2255255 19981208; US 5985582 A US 1997-987038 19971209; AU 730231 B AU 1998-95156 19981202; AU 2000072346 A Div ex AU 1998-95156 19981202, AU 2000-72346 20001218; AU 744025 B Div ex AU 1998-95156 19981202, AU 2000-72346 20001218
FDT AU 730231 B Previous Publ. AU 9895156; AU 2000072346 A Div ex AU 730231; AU 744025 B Previous Publ. AU 2000072346, Div ex AU 730231
PRAI US 1997-987038 19971209; AU 2000-72346 20001218
IC ICM **C12Q001-56**; **G01N033-86**; **G01N033-96**
ICS C08B037-10; C12P019-04; **C12Q001-44**; G01N021-78; **G01N033-50**
AB EP 927767 A UPAB: 20040408
NOVELTY - Determination of **antithrombin** III in a **plasma** sample comprises, combining the **plasma** sample with exogenous **thrombin** and with a heparin derivative (prepared by enzymatically digesting heparin) to form an assay mixture, forming a complex between the **antithrombin** III and the **thrombin**, determining the uncomplexed **thrombin**, and correlating the determined uncomplexed **thrombin** to the **antithrombin** III.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) determination of **antithrombin** III in a **plasma** sample comprising, preparing an assay mixture comprising the **plasma** sample, exogenous **thrombin**, and a heparin derivative, (effective for enhancing formation of a **thrombin**-**antithrombin** III complex and less effective than unmodified heparin for enhancing heparin cofactor II activity against **thrombin**), incubating the assay mixture, determining the uncomplexed **thrombin** in the incubated assay mixture and correlating the determined uncomplexed **thrombin** to the **antithrombin** III in the **plasma** sample;

(2) determination of **antithrombin** III in a **plasma** sample containing endogenous heparin cofactor II comprising, preparing an assay mixture comprising the **plasma** sample, exogenous **thrombin** and a heparin derivative, incubating the assay mixture, determining the uncomplexed **thrombin** in the incubated assay mixture and correlating the determined uncomplexed **thrombin** to **antithrombin** III in the **plasma** sample, where the endogenous heparin cofactor II contributes about 15% or less to the determined inhibition of **thrombin** by **antithrombin** III;

(3) a modified heparin comprising a heparin derivative effective for enhancing the **antithrombin** activity against **thrombin** and being less effective than unmodified heparin for enhancing heparin cofactor II activity against **thrombin**;

(4) the preparation of a heparin derivative comprising enzymatically digesting heparin with chondroitinase;

(5) a reagent useful in a **thrombin**-based, **antithrombin** III assay comprising, a lyophilized composition comprising **thrombin** and a heparin derivative (as above);

(6) a kit for a **thrombin** based **antithrombin** III assay, useful for determining **antithrombin** III in a **plasma** sample comprising, a diluent composition comprising chondroitinase ACI-treated heparin and an alkali metal-halide salt, a reagent composition comprising chondroitinase ACI-treated heparin, an alkali metal-halide salt and **thrombin** and a chromogenic **thrombin** substrate;

(7) the preparation of a high-calibrator reference **plasma** suitable for use as a **standard** for the determination of a **plasma** constituent comprising, obtaining a **normal** reference **plasma**, lyophilizing a volume, V1, of the **normal** reference **plasma**, and reconstituting the lyophilized **normal** reference **plasma** to form a reconstituted **plasma** of volume, V2, where the **ratio** of V1:V2 ranges from 7:8 to 1:8; and

(8) a reference **plasma** suitable for use as a **standard** for determination of a **plasma** constituent, the reference **plasma** comprising **antithrombin** III at more than 120% of the **normal**.

USE - The **method** is useful for evaluating the hemostasis of a patient of developing **thrombosis**, and especially, to diagnostic assays for determining the level of **antithrombin** III present in a **plasma** sample from a patient. The **method** is particularly employed with patients known to be or suspected of being at risk of **thrombosis** and especially those with an **antithrombin** deficiency e.g. genetic deficiencies (especially, Type I and Type II), and acquired deficiencies such as those occurring in consumptive **coagulopathies** (especially, DVT, DIC, pulmonary emboli), other disease states (especially, severe liver disease, nephrotic syndrome), surgery, preganancy, trauma and certain courses of therapy (e.g. L-asparaginase).

ADVANTAGE - The **antithrombin** III assay is not influenced by the **antithrombin** activity of heparin cofactor II, which can be

suitably performed with automated analyzers, and which are simpler to perform, maintaining sensitivity, accuracy, reproducibility and is relatively inexpensive (especially without using expensive and unstable reagents).
Dwg.0/7

FS CPI
FA AB; DCN
MC CPI: **B04-B04D4**; B04-C02E1; **B04-H19**; B04-L05; B04-N02; B11-C08E3; B12-K04A; D05-A02C; D05-C08; **D05-H09**
TECH UPTX: 19990806
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **Method**: The (modified) heparin derivative is prepared by enzymatically digesting heparin to form a (modified) heparin derivative and at least one (especially unsaturated) disaccharide, and the assay mixture is formed by combining the **plasma** sample with **thrombin** and with the modified heparin composition. The heparin derivative is prepared by enzymatically digesting heparin with a chondroitinase (especially chondroitinase ACI-digested heparin). The heparin derivative is at least two (especially 5) **times** less effective than unmodified heparin for enhancing heparin cofactor II activity against **thrombin**. The endogenous heparin cofactor II contributes about no more than 10 (especially 5) % to the determined inhibition of **thrombin** by **antithrombin** III. The **method** (7), has a **ratio** of V2:V1 of 3:4 - 1:4 (especially 2:3). The **normal** reference **plasma** comprises **antithrombin** III at a concentration of 90-110% of **normal** and at least 120 (especially 140) % of **normal**, reconstituted **plasma** comprising **antithrombin** III.
Preferred Reagent: The lyophilized composition comprises **thrombin** and a modified heparin composition prepared by enzymatically digesting heparin, especially by lyophilizing a reagent solution comprising 8-96 IU/ml **thrombin** and 0.5-6 U/ml heparin derivative.
ABEX UPTX: 19990806
EXAMPLE - ATIII assays were performed on each HCII-**normal** samples with protocols involving the heparin derivative. The HCII samples were diluted 1/40 in the heparin derivative diluent composition (25 mul **plasma** sample and 975 mul diluent composition), and equilibrated to 37 degreesC. 200 mul Of this mixture was mixed with 200 mul of the heparin-derivative-**thrombin** reagent composition and was also equilibrated to 37 degreesC to form an assay mixture. The assay mixture which included 175 mM sodium chloride was incubated for 2 minutes at 37 degreesC. 200 mul Of the chromogenic **thrombin** substrate was added to the incubated assay mixture and allowed to react with the uncomplexed **thrombin** for exactly 1 or 2 minutes, depending on the relative concentrations of **thrombin** and substrate, to form a developed assay mixture. The reactions were stopped using 200 mul glacial acetic acid or 2% citric acid. The absorbance of the developed assay mixture was read at OD405 using a spectrophotometer. A **standard** curve was prepared.

L62 ANSWER 22 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-279597 [24] WPIX
DNN N1999-209694 DNC C1999-082276
TI Determination of anti-**coagulation** potential of a sample.
DC B04 D16 S03
IN KRAUS, M
PA (DADE-N) DADE BEHRING MARBURG GMBH; (KRAU-I) KRAUS M
CYC 29
PI EP 915340 A1 19990512 (199924)* GE 18 G01N033-86 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
DE 19749197 A1 19990512 (199925) C12Q001-56 <--
AU 9891397 A 19990527 (199932) C12Q001-56 <--

CA 2252983 A1 19990507 (199942) EN C12Q001-56 <--
JP 11225796 A 19990824 (199944) 13 C12Q001-56 <--
US 2002019021 A1 20020214 (200214) C12Q001-56 <--
AU 751525 B 20020822 (200266) C12Q001-56 <--
US 2003207343 A1 20031106 (200374) C12Q001-56 <--

ADT EP 915340 A1 EP 1998-118971 19981007; DE 19749197 A1 DE 1997-1049197 19971107; AU 9891397 A AU 1998-91397 19981106; CA 2252983 A1 CA 1998-2252983 19981106; JP 11225796 A JP 1998-315511 19981106; US 2002019021 A1 US 1998-187035 19981106; AU 751525 B AU 1998-91397 19981106; US 2003207343 A1 Div ex US 1998-187035 19981106, US 2003-419104 20030421

FDT AU 751525 B Previous Publ. AU 9891397

PRAI DE 1997-19749197 19971107

IC ICM **C12Q001-56**; **G01N033-86**
ICS C07K014-00; C07K016-00; C08B037-10; C12N009-74; **G01N033-15**

ICA **G01N033-50**

AB EP 915340 A UPAB: 19990624
NOVELTY - Determination of anti-**coagulation** potential of a sample is carried out in the presence of exogeneous **thrombomodulin**.

DETAILED DESCRIPTION - Determination of anti-**coagulation** potential of a sample in the presence of an exogenous **thrombomodulin** comprises: (a) adding to the sample exogenous **thrombomodulin**, which can form a **protein C**-**activating**-complex with **thrombin**, whereby the **protein C** can be exogenous or endogenous, an **activator** for **thrombin**, where the **prothrombin** is either endogenous or exogenous, **phospholipids**, calcium ions and other reagents for the optimization of the **coagulation time** test; (b) starting the **prothrombin**-**activator** reaction; and (c) determining the formation of **thrombin** by either measuring the **time** of **thrombin** formation, **fibrin clot** formation or formation of labeled **thrombin.** INDEPENDENT CLAIMS are also included for: (1) a test kit used to carry out the **method** above; and (2) a **method** for determining anti-**thrombin** III activity of the **protein C** system of a sample, comprising the step described above.

USE - The **method** is used for the selective diagnosis of protein defects or protein lack in a patients sample (all claimed).

FS CPI EPI

FA AB; DCN

MC CPI: **B04-H19**; B04-N02; B11-C08E; **B12-K04A2**; **D05-H09**
EPI: **S03-E14H1**; **S03-E14H5**; **S03-E14H6**

TECH UPTX: 19990624
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **Method**: The **thrombin** formation is evaluated in contrast to **thrombin** formation without the addition of **protein C** to the sample; or by adding a test substance instead of **thrombomodulin.** The **thrombomodulin** used also promotes the inhibition of **thrombin** by anti-**thrombin** III. The concentration of the **activator** is such that **coagulation** takes place within 20-300 (especially 30-150) s. The **activators** are common **activators** used as derived from placenta, lung or brain. The **thrombinmodulin**, derived from human or animal sources is added separately from the **activator** to the sample. The **thrombin** inhibition caused by **thrombomodulin** can be reversed by binding of glycosamino glycan, especially heparin sulfate.

L62 ANSWER 23 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN **1999-095346** [08] WPIX

DNN **N1999-069309** DNC **C1999-028092**

TI Determining enzymatic activity of **blood coagulation**

factor XIII - by detecting degree of **fibrin** cross-linking formed by **blood coagulation** factor XIII using purified **fibrin** monomer.

DC B04 D16 S03

IN CHANG, S; CHUNG, S; HUH, J; KIM, H; LEE, J; SEONG, H; CHUNG, ; SEONG, ; CHANG, S J; CHUNG, S G; HUH, J W; KIM, H C; LEE, J S; SEONG, H M

PA (GREC) KOREA GREEN CROSS CORP

CYC 22

PI WO 9858078 A1 19981223 (199908)* EN 33 C12Q001-56 <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: JP US
EP 956363 A1 19991117 (199953) EN C12Q001-56 <--
R: AT CH DE FR GB LI SE
KR 99002006 A 19990115 (200011) G01N033-49 <--
JP 2000501295 W 20000208 (200018) 20 C12Q001-56 <--
KR 222292 B1 19991001 (200108) G01N033-49 <--
JP 3193728 B2 20010730 (200146) 8 C12Q001-56 <--
US 6406874 B1 20020618 (200244) C12Q001-56 <--
EP 956363 B1 20031001 (200365) EN C12Q001-56 <--
R: AT CH DE FR GB LI SE
DE 69818639 E 20031106 (200381) C12Q001-56 <--

ADT WO 9858078 A1 WO 1998-KR160 19980616; EP 956363 A1 EP 1998-929875 19980616, WO 1998-KR160 19980616; KR 99002006 A KR 1997-25516 19970618; JP 2000501295 W WO 1998-KR160 19980616, JP 1999-504191 19980616; KR 222292 B1 KR 1997-25516 19970618; JP 3193728 B2 WO 1998-KR160 19980616, JP 1999-504191 19980616; US 6406874 B1 WO 1998-KR160 19980616, US 1999-242436 19990217; EP 956363 B1 EP 1998-929875 19980616, WO 1998-KR160 19980616; DE 69818639 E DE 1998-618639 19980616, EP 1998-929875 19980616, WO 1998-KR160 19980616

FDT EP 956363 A1 Based on WO 9858078; JP 2000501295 W Based on WO 9858078; JP 3193728 B2 Previous Publ. JP 200001295, Based on WO 9858078; US 6406874 B1 Based on WO 9858078; EP 956363 B1 Based on WO 9858078; DE 69818639 E Based on EP 956363, Based on WO 9858078

PRAI KR 1997-25516 19970618

IC ICM **C12Q001-56**; **G01N033-49**
ICS **C12Q001-37**; **C12Q001-48**; **G01N033-573**; **G01N033-72**; **G01N033-86**

AB WO 9858078 A UPAB: 19990224
Determining the enzymatic activity of **blood coagulation** factor XIII by detecting the degree of **fibrin** cross-linking formed by the **blood coagulation** factor XIII using purified **fibrin** monomer as a substrate which is free of contaminating **blood coagulation** factor XIII.
USE - The **method** is especially used for determining the activity of transglutaminase (claimed).
Dwg.0/5

FS CPI EPI

FA AB

MC CPI: **B04-B04D3**; **B04-B04D5**; **B04-H19**; B04-L04; B11-C08E; B12-K04A; **D05-H09**
EPI: **S03-E14H**; **S03-E14H4**

L62 ANSWER 24 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN **1999-036163** [04] WPIX

DNN **N1999-027154** DNC **C1999-011034**

TI Diagnosis of **thrombophilia** - by determining **anticoagulatory** activity of **thrombin.**

DC B04 D16 J04 S03

IN HUND, S; MUELLER-BERGHAUS, G; POETZSCH, B

PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN; (KERC-N) KERCKHOFF-KLINIK GMBH

CYC 22

PI DE 19724239 A1 19981210 (199904)* 7 G01N033-50 <--

WO 9857178 A1 19981217 (199905) GE G01N033-86 <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US
EP 990157 A1 20000405 (200021) GE G01N033-86 <--
R: AT CH DE ES FR GB IT LI NL
ADT DE 19724239 A1 DE 1997-1024239 19970609; WO 9857178 A1 WO 1998-EP3407 19980608; EP 990157 A1 EP 1998-934924 19980608, WO 1998-EP3407 19980608
FDT EP 990157 A1 Based on WO 9857178
PRAI DE 1997-19724239 19970609
IC ICM **G01N033-50**; **G01N033-86**
ICS **C12Q001-56**; **G01N033-53**; **G01N033-577**; **G01N033-68**
AB DE 19724239 A UPAB: 19990127
Diagnosing **thrombophilia** [congenital predisposition to **thrombosis**] comprises determining the **anticoagulatory** activity of **thrombin** in a **blood** or **plasma** sample.
ADVANTAGE - In some patients clinically diagnosed as **thrombophilic** [9 out of 57 in an example], interaction of **thrombin-thrombomodulin** complex with **protein C** results in less **activated protein C** (APC) formation than would be expected from the amount of **thrombin** present.
Dwg.0/2
FS CPI EPI
FA AB
MC CPI: **B04-B04D4**; **B04-H19**; B04-N02; B11-C08; **B12-K04A2**; **D05-H09**; J04-B01
EPI: **S03-E14H1**; **S03-E14H4**

L62 ANSWER 25 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **1998-448979** [39] WPIX
DNN **N1998-350152** DNC **C1998-136190**
TI Evaluation of reaction kinetics - using modified threshold **method**
.
DC B04 D16 S03
IN MEYERS, W
PA (DADE-N) DADE BEHRING MARBURG GMBH; (BEHW) BEHRING DIAGNOSTICS GMBH
CYC 27
PI EP 861687 A1 19980902 (199839)* GE 15 B01J019-00
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
DE 19707897 A1 19980910 (199842) G01N037-00
JP 10253636 A 19980925 (199849) 12 G01N033-86 <--
CA 2230546 A 19980827 (199903) C12Q001-00 <--
US 6245569 B1 20010612 (200135) G01N033-00 <--
ADT EP 861687 A1 EP 1998-101330 19980127; DE 19707897 A1 DE 1997-1007897 19970227; JP 10253636 A JP 1998-45535 19980226; CA 2230546 A CA 1998-2230546 19980226; US 6245569 B1 US 1998-30887 19980226
PRAI DE 1997-19707897 19970227
IC ICM B01J019-00; **C12Q001-00**; **G01N033-00**; **G01N033-86**; G01N037-00
ICS C12M001-34; **C12Q001-56**; G01N021-27; G01N021-75; G01N031-00; **G01N033-49**; **G01N033-50**; **G01N033-557**; G06F019-00
AB EP 861687 A UPAB: 19981028
Method for evaluating reaction kinetics comprises: determining the variation in a reaction-dependent parameter and measuring the **time** (T) required for the parameter to exceed a limiting value (d); establishing reaction-specific values for an initial value d0, a maximum value dmax (>d0) and a step number n, thereby establishing a step width ds = (dmax-d0)/n; for the region d = d0 to dmax, determining the value Tn for each dn = (d0+(ds)*n); from the series of values T0 to Tmax,

determining the differences Di = Ti-Ti-1 for i = 1,...,n; from the values D1,..n, determining the highest value Dmax and the lowest value Dmin and calculating the quotient Q = Dmax/Dmin; and using only those measurements for which Q at most Q0 for further evaluation.
USE - For determining **blood clotting** parameters, especially **prothrombin time.**
Dwg.0/14
FS CPI EPI
FA AB
MC CPI: **B04-B04D5; B04-H19**; B11-C08; B12-K04A; **D05-H09**
EPI: S03-E04A1; **S03-E14H; S03-E14H1**

L62 ANSWER 26 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **1998-011964** [02] WPIX
DNN **N1998-009444** DNC **C1998-004360**
TI Measuring **thrombin** activity for aggregation reagent for assay of **blood coagulation** factor - involves supplying insoluble carrier with fibrinogen to examined object.
DC B04 D16 S03
PA (TOKU) TOKUYAMA SODA KK
CYC 1
PI JP 09266798 A 19971014 (199802)* 5 C12Q001-56 <--
ADT JP 09266798 A JP 1996-77301 19960329
PRAI JP 1996-77301 19960329
IC ICM **C12Q001-56**
ICS **G01N033-50; G01N033-86**
AB JP 09266798 A UPAB: 19980112
Measuring **thrombin** activity for aggregation reagent for assay of **blood coagulation** factor involves supplying an insoluble carrier with fibrinogen to an examined object. Then **thrombin** activity is determined by measuring the amount of aggregation of the carrier.
ADVANTAGE - **Thrombin** activity measurement is reduced.
Dwg.1/3
FS CPI EPI
FA AB; GI
MC CPI: **B04-B04D5; D05-H09**
EPI: **S03-E14H**

L62 ANSWER 27 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **1998-009937** [02] WPIX
DNN **N1998-007727** DNC **C1998-003717**
TI **Method** for performing **blood** tests - on **blood** samples treated with **thrombin** inhibitor, useful to perform wide rage of tests.
DC B04 D16 S03
IN MELBER, K; MENSSEN, H D; STRASSER, A W M; THIEL, E; STRASSER, A W
PA (RHEI-N) RHEIN BIOTECH GES NEUE BIOTECHNOLOGISCHE; (UYFR-N) UNIV FRANKLIN BENJAMIN; (UYBE-N) UNIV BERLIN FREIE; (MENS-I) MENSSEN H D; (THIE-I) THIEL E
CYC 67
PI DE 19620443 A1 19971127 (199802)* 9 G01N033-50 <--
WO 9744661 A1 19971127 (199802) GE 33 G01N033-50 <--
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AU BA BB BG BR CA CN CU CZ EE GE HU IL IS JP KP KR LC LK LR LT LV MG MK MN MX NO NZ PL RO SG SI SK TR TT UA US UZ VN
AU 9728936 A 19971209 (199824) G01N033-50 <--
DE 19620443 C2 19980917 (199841) G01N033-50 <--
EP 912891 A1 19990506 (199922) GE G01N033-50 <--
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 11511856 W 19991012 (199954) 26 G01N033-86 <--

EP 912891 B1 20021016 (200276) GE G01N033-50 <--
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
DE 59708506 G 20021121 (200277) G01N033-50 <--
US 6521460 B1 20030218 (200317) G01N033-86 <--
ES 2185937 T3 20030501 (200341) G01N033-50 <--
JP 3523883 B2 20040426 (200428) 11 G01N033-86 <--

ADT DE 19620443 A1 DE 1996-1020443 19960521; WO 9744661 A1 WO 1997-EP2343 19970507; AU 9728936 A AU 1997-28936 19970507; DE 19620443 C2 DE 1996-1020443 19960521; EP 912891 A1 EP 1997-923007 19970507, WO 1997-EP2343 19970507; JP 11511856 W JP 1997-540286 19970507, WO 1997-EP2343 19970507; EP 912891 B1 EP 1997-923007 19970507, WO 1997-EP2343 19970507; DE 59708506 G DE 1997-508506 19970507, EP 1997-923007 19970507, WO 1997-EP2343 19970507; US 6521460 B1 WO 1997-EP2343 19970507, US 1999-180806 19990208; ES 2185937 T3 EP 1997-923007 19970507; JP 3523883 B2 JP 1997-540286 19970507, WO 1997-EP2343 19970507

FDT AU 9728936 A Based on WO 9744661; EP 912891 A1 Based on WO 9744661; JP 11511856 W Based on WO 9744661; EP 912891 B1 Based on WO 9744661; DE 59708506 G Based on EP 912891, Based on WO 9744661; US 6521460 B1 Based on WO 9744661; ES 2185937 T3 Based on EP 912891; JP 3523883 B2 Previous Publ. JP 11511856, Based on WO 9744661

PRAI DE 1996-19620443 19960521

IC ICM **G01N033-50**; **G01N033-86**
ICS **C12Q001-00**; G01N001-18; **G01N033-53**; **G01N033-569**; **G01N033-80**; G01N035-00

ICA **G01N033-49**

AB DE 19620443 A UPAB: 19980112
Method for performing **blood** tests comprises treating a freshly collected **blood** sample with at least 1 **thrombin** inhibitor and using the sample to determine **blood** chemistry and optionally **haematology** parameters.
ADVANTAGE - The same sample can be used to perform a wide range of tests. Only one **blood** sample has to be taken, which is of benefit to patients which may lack sufficient **blood** already..
Dwg.0/0

FS CPI EPI

FA AB

MC CPI: **B04-B04D4**; B04-B04M; B11-C08E; B12-K04A; **D05-H09**
EPI: S03-E13B2; **S03-E14H**; **S03-E14H4**; S03-E15

L62 ANSWER 28 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 1997-087078 [08] WPIX

DNN N1997-071762 DNC C1997-028266

TI Determn. **thrombotic** risk - by detection of **Protein-C** and Protein-S activity.

DC B04 D16 S03

IN CAMPBELL, P A; PREDA, L

PA (INLI) INSTRUMENTATION LAB SPA

CYC 22

PI WO 9642018 A1 19961227 (199708)* EN 28 G01N033-86 <--
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP MX US
EP 830608 A1 19980325 (199816) EN G01N033-86 <--
R: AT BE CH DE DK ES FR GB IT LI NL SE
US 5780255 A 19980714 (199835) C12Q001-37 <--
JP 11504718 W 19990427 (199927) 26 G01N033-86 <--
MX 9709961 A1 19981001 (200019) G01N033-86 <--
EP 830608 B1 20001004 (200050) EN G01N033-86 <--
R: AT BE CH DE DK ES FR GB IT LI NL SE
DE 69610558 E 20001109 (200064) G01N033-86 <--
ES 2152531 T3 20010201 (200112) G01N033-86 <--
JP 3248621 B2 20020121 (200207) 12 G01N033-86 <--

ADT WO 9642018 A1 WO 1996-US9036 19960606; EP 830608 A1 EP 1996-919107 19960606, WO 1996-US9036 19960606; US 5780255 A US 1995-488510 19950609;

JP 11504718 W WO 1996-US9036 19960606, JP 1997-503149 19960606; MX 9709961 A1 MX 1997-9961 19971209; EP 830608 B1 EP 1996-919107 19960606, WO 1996-US9036 19960606; DE 69610558 E DE 1996-610558 19960606, EP 1996-919107 19960606, WO 1996-US9036 19960606; ES 2152531 T3 EP 1996-919107 19960606; JP 3248621 B2 WO 1996-US9036 19960606, JP 1997-503149 19960606

FDT EP 830608 A1 Based on WO 9642018; JP 11504718 W Based on WO 9642018; EP 830608 B1 Based on WO 9642018; DE 69610558 E Based on EP 830608, Based on WO 9642018; ES 2152531 T3 Based on EP 830608; JP 3248621 B2 Previous Publ. JP 11504718, Based on WO 9642018

PRAI US 1995-488510 19950609

REP EP 236985; EP 406971; EP 434377; EP 445626; EP 633473; WO 9310261

IC ICM **C12Q001-37**; **G01N033-86**
ICS C12N009-48; C12N009-74; **C12Q001-56**; **G01N033-50**

AB WO 9642018 A UPAB: 19970220

Determining **thrombotic** risk in a subject comprises: (1) (a) treating first **plasma** samples (FPS) with a first reagent to induce or **activate coagulation**, a second reagent (SR) which **activates** endogenous **protein C** in the **plasma** and a third reagent (TR) comprising calcium salts, **phospholipids** and/or tissue **thromboplastin**;

(b) treating a second **plasma** sample (SPS) with FR, a buffer or other material which does not **activate protein C** and TR;

(c) measuring the **time** and/or **rate** necessary for conversion of endogenous fibrinogen to **fibrin** in both samples;

(d) calculating the difference in **ratio** between the **time** and/or **rate** of the samples;

(e) repeating steps (a)-(c) on a sample of **normal** control **plasma**, and

(f) determining the difference or **ratio** in the **times** and/or **rates** obtd. in steps (d) and (e) where the difference is indicative of the **thrombotic** risk; or

(2)

(a') treating FPS with a first reagent (FR') comprising a synthetic substrate (ss) and SR;

(b') treating SPS with FR' and a buffer or other material which does not **activate protein C**;

(c') measuring the **rate** of hydrolysis of ss in both samples;

(d') calculating the difference between the **rates**;

(e') repeating steps (d')-(c') on **normal** control **plasma**, and

(f') determining the difference or **ratio** in the **rates** obtd. in steps (d') and (e'), the difference being indicative of **thrombotic** risk.

Also claimed are kits comprising a first container comprising:

(1) (a) a first container comprising FR, SR and TR and (b) a second container for adding a second **plasma** sample, FR, buffer or other material which does not **activate protein C** and TC, and

(2) (a') a first container comprising FR', and SR; (b') a second container for adding to a SPS FR' and a buffer or other material which does not **activate protein C.**

USE - The global test can be a diagnostic aid for the evaluation of **thrombotic** risk in patients suffering from hereditary and non-hereditary **thrombophilia**, i.e. disorders of the **haemopoietic** system in which there is a tendency toward the occurrence of **thrombosis**, or otherwise in patients undergoing particularly pharmacologic treatments such as extroprogestinics. Additionally patients undergoing surgery can be evaluated to determine **thrombotic** risk. The test is used in vitro to diagnose **clotting** anomalies involved in the inhibitory system, due to

either **protein C** (PC) or S (PS) deficiency or the presence of molecular anomalies of Factor Va or to the presence of anti-a PC antibodies.
Dwg.0/1
FS CPI EPI
FA AB; DCN
MC CPI: B04-B01B; B04-B04G; **B04-H19**; B04-N02; B05-A01B; B05-B01P; B11-C08D3; B12-K04A; **D05-H09**
EPI: **S03-E14H1**; **S03-E14H5**

L62 ANSWER 29 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1996-200281 [20] WPIX
DNN N1996-168115 DNC C1996-063239
TI Determination of individual's inflammation index in anti-**coagulated** whole **blood** - by using whole **blood** fibrinogen and **haematocrit** or **haemoglobin** measurements.
DC B04 S03
IN BULL, B S; LEVINE, R A; WARDLAW, S C
PA (BULL-I) BULL B S; (LEVI-I) LEVINE R A; (WARD-I) WARDLAW S C; (LEVI-I) LEVIN R A; (WARD-I) WARDROW S C
CYC 24
PI

US 5506145	A	19960409 (199620)*		6	G01N033-86	<--
EP 715170	A2	19960605 (199627)	EN	6	G01N033-49	<--
R: AT BE CH DE DK ES FR GB GR IE IT LI NL PT SE						
AU 9520211	A	19960613 (199631)			G01N033-72	<--
NO 9504897	A	19960603 (199631)			G01N033-68	<--
JP 08166389	A	19960625 (199635)		7	G01N033-72	<--
CA 2149580	A	19960603 (199639)			C12Q001-56	<--
FI 9505784	A	19960603 (199639)			G01N033-49	<--
CN 1123914	A	19960605 (199747)			G01N033-68	<--
TW 321721	A	19971201 (199814)			G01N033-49	<--
AU 690972	B	19980507 (199830)			G01N033-72	<--
RU 2122212	C1	19981120 (200014)			G01N033-86	<--

ADT US 5506145 A US 1994-348345 19941202; EP 715170 A2 EP 1995-118964 19951201; AU 9520211 A AU 1995-20211 19950523; NO 9504897 A NO 1995-4897 19951201; JP 08166389 A JP 1995-170802 19950706; CA 2149580 A CA 1995-2149580 19950517; FI 9505784 A FI 1995-5784 19951201; CN 1123914 A CN 1995-108425 19950714; TW 321721 A TW 1995-106027 19950613; AU 690972 B AU 1995-20211 19950523; RU 2122212 C1 RU 1995-113187 19950714
FDT AU 690972 B Previous Publ. AU 9520211
PRAI US 1994-348345 19941202
REP No-SR.Pub
IC ICM **C12Q001-56**; **G01N033-49**; **G01N033-68**; **G01N033-72**; **G01N033-86**
ICS G01N015-05; **G01N033-53**
ICA A61K049-00
AB US 5506145 A UPAB: 19960520
Deg of mammalian donor systemic inflammation is determined from a sample of donor **anticoagulated** whole **blood** A sample of the **blood** is drawn from a donor into a transparent tube (2) containing an elongated float (4). The sample is centrifuged in the tube. The amount of fibrinogen/**fibrin** in the **blood** sample in the tube is measured. A **haematocrit** or **haemoglobin** value for the **blood** sample in the tube is determined. A number I, indicative of the degree of systemic inflammation, is computed by solving equation (i) I = a(f) + b(h) + c where f is the measured fibrinogen/**fibrin** level in the sample; h is the determined **haematocrit** or **haemoglobin** value in the sample; and a, b and c are empirically derived constants. The numerical value of I is correlated with the deg. of mammalian donor systemic inflammation.
USE - **Method** determines the presence or absence of inflammatory condition in patient by quantifying fibrinogen content and

haematocrit or **haemoglobin** content in sample of patient's **blood.** Patient may be human, or process may be used in veterinary work.

ADVANTAGE - **Method** is not susceptible to systemic abnormalities that render Westergren erythrocyte sedimentation **rate method** unreliable. Amount of **blood** required is small and **time** required for procedure is short.

Dwg.1/1

FS CPI EPI
FA AB; GI
MC CPI: **B04-B04D2**; B11-C08E; B12-K04A
EPI: **S03-E14H**

L62 ANSWER 30 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1996-130880 [14] WPIX
DNN N1996-109976 DNC C1996-040926
TI Determn. of fibrinogen concentration in undiluted **plasma** sample - comprises addition of novel reagent containing **thrombin** or protease, in presence of high concentration of salt.
DC B04 D16 S03
IN ENOMOTO, M
PA (NNTR) NIPPON SHOJI KAISHA LTD; (AZWE-N) AZWELL INC; (NNTR) NIPPON SHOJI KK
CYC 5
PI

EP 699909	A2	19960306	(199614)*	EN	G01N033-86	<--
R: DE FR GB						
JP 08070895	A	19960319	(199621)	10	C12Q001-56	<--
EP 699909	A3	19960619	(199635)		G01N033-86	<--
US 5851836	A	19981222	(199907)		G01N033-49	<--
JP 2994557	B2	19991227	(200006)	10	C12Q001-56	<--
EP 699909	B1	20011128	(200201)	EN	G01N033-86	<--
R: DE FR GB						
DE 69524161	E	20020110	(200211)		G01N033-86	<--

ADT EP 699909 A2 EP 1995-113736 19950901; JP 08070895 A JP 1994-209940 19940902; EP 699909 A3 EP 1995-113736 19950901; US 5851836 A US 1995-521868 19950831; JP 2994557 B2 JP 1994-209940 19940902; EP 699909 B1 EP 1995-113736 19950901; DE 69524161 E DE 1995-624161 19950901, EP 1995-113736 19950901
FDT JP 2994557 B2 Previous Publ. JP 08070895; DE 69524161 E Based on EP 699909
PRAI JP 1994-209940 19940902
REP 1.Jnl.Ref; EP 537490; EP 570354; EP 632270; JP 05219993; US 5292664; WO 9407145
IC ICM C12Q001-56; **G01N033-49**; **G01N033-86**
ICS C12Q001-37
AB EP 699909 A UPAB: 19960405

Method for determn. of fibrinogen (I) concentration comprises: (1) addition of **thrombin**, or a protease having similar activity, to an undiluted sample (if **plasma**) in a reaction mixture containing a salt (II) at high concentration, then (2) measurement of the **coagulation time**. The concentration of (II) is set at a level giving a **coagulation time** of 5-100 secs. at 37deg.C. using a mixture of a fibrinogen-containing sample (275 mg/dl) and a reagent (III) containing **thrombin** (100NIHU/ml and HEPES (RTM:buffer) (100mM; pH 7.35;) the volume **ratio** sample (III) being from 1-2 (pref. 1:1.0-1.8). Salt (II) is 1 of :- NaCl (0.25-3.0 concentration), NaBr (0.1-1.0), NaI (0.1-0.4), KCl (0.25-1.5), KBr (0.1-1.0), KI (0.1-0.4), MgCl2 (0.04-0.25), CaCl2 (0.04-0.25). A pref. (III) contains 1.0-2.5M NaCl and 0.1-0.8M NaBr, and an especially pref. reaction mixture comprises 0.25-1.0M NaCl, 0.05-0.2 KF or NAF, 2-50 mM Na citrate and, as a discrepancy preventive (IV), 0.001-0.5 w/v% of a surfactant. Also claimed are reagents per se. These comprise salt a t high concentration (set at a level giving a **coagulation time**

of 5-100 secs., measured under conditions as described above) and 20-500 NIHU/ml of **thrombin** or a protease. An especially pref. reagent comprises 40-200 (NIHU/ml. **thrombin**, 30-200 ml. buffer (pH 7.0-8.0), 1.0-3.5M NaCl and 0.3-1.0 MNaBr. Alternatively, 2 reagents may be used, a first comprising (IV) and a second consisting of **thrombin** or a protease and (II) may be in the first or second reagent.

ADVANTAGE - The **method** uses undiluted samples of **plasma**, and conventional equipment for measurement of **coagulation time**. Samples having a low content of (I) can be assayed using a **normal** amount of **thrombin** without use of expensive peptides or prolonging the **coagulation time**. The results correlate well with those obtd. by the conventional dilution **method** and can be used for routine **blood** tests.

Dwg.0/9

FS CPI EPI

FA AB; DCN

MC CPI: **B04-B04D4**; **B04-H19**; B04-L05C; B05-A01A; B05-A01B; B11-C08E; B12-K04; D05-A02C; **D05-H09**
EPI: **S03-E14H**

L62 ANSWER 31 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN **1995-233339** [31] WPIX

DNN **N1995-181839** DNC **C1995-107722**

TI Determn. of **thrombin**-induced **platelet** aggregation in presence of **fibrin** - comprises use of **fibrin** aggregation inhibitor to suppress **fibrin clot** formation.

DC B04 D16 S03

IN REERS, M

PA (DADE-N) DADE BEHRING MARBURG GMBH; (BEHW) BEHRINGWERKE AG

CYC 20

PI	EP 661383	A2	19950705 (199531)*	GE	5	C12Q001-56	<--
	R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE						
	DE 4344919	A1	19950706 (199532)		5	C12Q001-56	<--
	AU 9481788	A	19950706 (199534)			C12N009-99	
	CA 2138931	A	19950701 (199539)			C12Q001-56	<--
	JP 07203994	A	19950808 (199540)		4	C12Q001-56	<--
	US 5563041	A	19961008 (199646)		6	C12Q001-56	<--
	EP 661383	A3	19971217 (199818)			C12Q001-56	<--
	AU 702099	B	19990211 (199918)			C12N009-99	
	EP 661383	B1	20010321 (200117)	GE		C12Q001-56	<--
	R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE						
	DE 59409698	G	20010426 (200124)			C12Q001-56	<--
	ES 2155842	T3	20010601 (200137)			C12Q001-56	<--

ADT EP 661383 A2 EP 1994-119803 19941215; DE 4344919 A1 DE 1993-4344919 19931230; AU 9481788 A AU 1994-81788 19941229; CA 2138931 A CA 1994-2138931 19941222; JP 07203994 A JP 1994-326514 19941228; US 5563041 A US 1994-365759 19941229; EP 661383 A3 EP 1994-119803 19941215; AU 702099 B AU 1994-81788 19941229; EP 661383 B1 EP 1994-119803 19941215; DE 59409698 G DE 1994-509698 19941215, EP 1994-119803 19941215; ES 2155842 T3 EP 1994-119803 19941215

FDT AU 702099 B Previous Publ. AU 9481788; DE 59409698 G Based on EP 661383; ES 2155842 T3 Based on EP 661383

PRAI DE 1993-4344919 19931230

REP EP 336353; EP 537490; US 5246832

IC ICM C12N009-99; **C12Q001-56**
ICS A61K035-14; C07K005-08; C07K005-10; C07K007-06; C12N009-48; C12N009-74; **C12Q001-00**; **G01N033-48**; **G01N033-49**; **G01N033-86**

AB EP 661383 A UPAB: 19950810
In the qualitative or quantitative determn. of **thrombin**-induced

platelet aggregation in the presence of **fibrin**, interference from **fibrin clot** formation is suppressed with a **fibrin**-aggregation inhibitor (I). Also claimed is a diagnostic reagent comprising **thrombin** and (I).
USE - The assay may be used to determine the **platelet** aggregation inhibitory activity of **thrombin** inhibitors.
ADVANTAGE - (I) inhibits **fibrin clot** formation at high **thrombin** concns. without inhibiting **platelet** aggregation.
Dwg.0/2

FS CPI EPI
FA AB; DCN
MC CPI: B04-C01; B04-M01; **B12-K04A2**; D05-A02C
EPI: **S03-E14H1**; S03-F03
ABEQ US 5563041 A UPAB: 19961115
A **method** for the qualitative or quantitative determination of **platelet** aggregation induced by **thrombin** in the presence of **fibrin**, wherein the formation of an interfering **fibrin clot** is prevented by the presence of an inhibitor of **fibrin** aggregation and the experimentally induced **platelet** aggregation is unaffected.
Dwg.0/2

L62 ANSWER 32 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **1995-061015** [08] WPIX
DNN **N1995-048479** DNC **C1995-027174**
TI **Method** for the quantification of active-plasminogen-**activator**-inhibitor-type-1 - present in a sample of **blood** or **plasma** is useful in the field of **haemostasis.**
DC B04 D16 S03
IN NIEUWENHUIZEN, W
PA (**ALKU**) **AKZO NOBEL NV**
CYC 23
PI WO 9501452 A1 19950112 (199508)* EN 41 C12Q001-56 <--
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA FI JP KR US
AU 9473844 A 19950124 (199520) C12Q001-56 <--
EP 706580 A1 19960417 (199620) EN C12Q001-56 <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
JP 08512133 W 19961217 (199710) 43 G01N033-53 <--
US 5753457 A 19980519 (199827) C12Q001-06 <--
ADT WO 9501452 A1 WO 1994-EP2127 19940628; AU 9473844 A AU 1994-73844 19940628; EP 706580 A1 EP 1994-923704 19940628, WO 1994-EP2127 19940628; JP 08512133 W WO 1994-EP2127 19940628, JP 1995-503274 19940628; US 5753457 A WO 1994-EP2127 19940628, US 1996-481284 19960221
FDT AU 9473844 A Based on WO 9501452; EP 706580 A1 Based on WO 9501452; JP 08512133 W Based on WO 9501452; US 5753457 A Based on WO 9501452
PRAI EP 1993-201880 19930628
REP 06Jnl.Ref; EP 339302; EP 450086; WO 8600413; WO 890005; WO 9323561
IC ICM **C12Q001-06**; **C12Q001-56**; **G01N033-53**
ICS **G01N033-566**; **G01N033-86**
AB WO 9501452 A UPAB: 19950301
Quantification of active plasminogen-**activator**-inhibition-type-1 (I) present in a sample comprises taking 2 portions from the sample and: (a) determining in 1 portion a valve corresp. to the total amount of complex between (I) and plasminogen **activator** (PA), the so-called PA-(I) complex with PA already present and the moment of sampling; and (b) calculating the amount of PA-(I) present at the moment of sampling; (c) determining in the other portion a value corresp. to the total amount of (II) present after addition of an excess of the active form of tissue type PA (t-PA) to the portion; and (d) calculating the amount of PA-(I) present after addition of an excess of the active form of t-PA to the portion; and (e) subtracting the total amount of complex from the total amount of PA-(I)

resulting in the amount of active (I) that was present at the moment of sampling in a volume of the sample equivalent to the volume of the portions, where the portion of step (a) is contacted with means for inhibiting complexation of PA with (I) from the moment of sampling through step (a). Step (a) comprises: (i) contacting the portion with 1 immobilised capturing agent (CAP), which (1) is directed at PA partic. of the PA-(I) complex and (2) is present in an amount and with a specificity sufficient for the mol. forms of PA, pref. of the PA-(I) complex present in the portion to be complexed to it; (ii) contacting the portion with 1 tagging agent (TAG) which: (1) is provided with a detectable marker (*); (2) is directed at plasminogen-**activation**-inhibitor (PAI), pref. PAI of PAI-(I) and (3) is present in an amount and with a specificity sufficient for the mol. forms of (I) present in the portions to be complexed to it; (iii) carrying out appropriate incubation and washing steps; (iv) determining a value corresp. to an amount of (*) that has been bound by an immobilised CAP. Step (c) comprises: (i) contacting the other portion with an excess of the active form of t-PA, thereby allowing non-bound active (I) present in the portion before the addition to form PA-(I); (ii) contacting this portion with TAG and CAP as in step (a), (iii) subsequently determining a value corresp. to the amount of (*) that has been bound to the immobilised CAP. Also claimed are: (A) use of a t-PA determn. assay to determine the complexed form of t-PA in a **method** for determining the specific known concentration of PA-(I) in the reference sample to

be used; (B) use of a **method** comprising: (1) subjecting the reference sample to conditions such that virtually all t-PA present is converted to t-PA-(I) co

Dwg.4/4

FS CPI EPI

FA AB; GI

MC CPI: **B04-B04D4**; **B04-B04D5**; B04-G21; B04-L03B; B11-C07A4; **B12-K04A2**; B14-D07C; **D05-H09**; D05-H10; D05-H11A
EPI: **S03-E14H1**

L62 ANSWER 33 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 1994-007456 [01] WPIX

CR 1994-007188 [01]

DNC C1994-002979

TI Test for quantitative **thrombin time** - using **plasma** dilutions, excess fibrinogen and **thrombin**, giving more accurate results than **standard** tests.

DC B04

IN ALVING, B; HENDRICKS, G; REID, T; ALVING, B M; REID, T J

PA (USSA) US DEPT OF ARMY; (ALVI-I) ALVING B M; (REID-I) REID T J

CYC 19

PI WO 9325578 A1 19931223 (199401)* EN 30 C07K007-10
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9347681 A 19940104 (199417) C07K007-10
JP 08501682 W 19960227 (199643) 29 C12Q001-56 <--

ADT WO 9325578 A1 WO 1993-US5315 19930603; AU 9347681 A AU 1993-47681 19930603; JP 08501682 W WO 1993-US5315 19930603, JP 1994-501586 19930603

FDT AU 9347681 A Based on WO 9325578; JP 08501682 W Based on WO 9325578

PRAI US 1992-893631 19920605; US 1993-21033 19930222

REP 2.Jnl.Ref; US 4379142; US 4496653; US 4767742; US 4952562; US 5019393; US 5118790; US 5187102; US 5196404

IC ICM C07K007-10; **C12Q001-56**
ICS A61K009-22; A61K031-445; A61K037-00; A61K037-02; A61K037-43; C07K007-08; **G01N033-50**; **G01N033-86**

AB WO 9325578 A UPAB: 19950223
(A) quantitating **plasma** levels of specific inhibitors of

thrombin, comprising: (a) preparing serial dilutions of a **thrombin**-specific inhibitor (TSI) in known concns. to give samples; (b) mixing the samples with purified human fibrinogen (PHF); (c) adding purified human alpha-**thrombin** (PHAT) to the samples prepared in (b); (d) measuring the **clotting times** of the solns. in (c); (e) plotting a **standard** curve from the effect of TSI based on the results obtained in (d); (f) diluting a **plasma** sample from patients receiving a TSI; (g) mixing the patient samples with a solution of fibrinogen of step (f) (sic); (h) adding a **thrombin** solution to the samples prepared in step (g); (i) measuring the **clotting times** of the solns. of step (h); and (j) determining the concentration of the inhibitor in the patient samples using the **standard** curve.

USE/ADVANTAGE - The new **method** of measuring **thrombin time** is not affected by the presence of abnormal **plasmas** which cause prolongation of **standard** tests. The **method** can be performed on **standard** laboratory instruments, and are fast and inexpensive. The **method** can be used in analysis of **thrombosis.**

Dwg.0/4

Dwg.0/4

FS CPI

FA AB

MC CPI: **B04-B04D2**; **B04-H19**; B11-C07; **B12-K04A2**

L62 ANSWER 34 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN **1993-395336** [49] WPIX

DNN **N1993-305443** DNC **C1993-176033**

TI Determining risk of **thrombosis** - by measuring pro-**coagulant** activity of **platelets**, namely resting activity and/or excitability of **platelets.**

DC B04 D16 S03

IN HEMKER, H C; WAGENVOORD, R J

PA (BAXT) BAXTER DIAGNOSTICS INC; (DADE-N) DADE PROD AG; (DADE-N) DADE PRODN AG

CYC 21

PI	US 5266462	A	19931130 (199349)*		29	C12Q001-56	<--
	WO 9324840	A1	19931209 (199350)	EN	63	G01N033-86	<--
	RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE						
	W: AU CA JP						
	AU 9344090	A	19931230 (199415)			G01N033-86	<--
	EP 605674	A1	19940713 (199427)	EN		G01N033-86	<--
	R: AT BE CH DE DK ES FR GB IE IT LI NL SE						
	JP 06509479	W	19941027 (199502)			C12Q001-56	<--
	AU 658073	B	19950330 (199521)			C12Q001-56	<--
	CA 2114719	C	19970826 (199748)			C12Q001-56	<--
	EP 605674	B1	19980121 (199808)	EN	40	G01N033-86	<--
	R: AT BE CH DE DK ES FR GB IE IT LI NL SE						
	DE 69316572	E	19980226 (199814)			G01N033-86	<--
	ES 2114053	T3	19980516 (199826)			G01N033-86	<--
	JP 3143694	B2	20010307 (200116)		31	C12Q001-56	<--

ADT US 5266462 A US 1992-892865 19920603; WO 9324840 A1 WO 1993-US5436 19930603; AU 9344090 A AU 1993-44090 19930603; EP 605674 A1 EP 1993-912364 19930603, WO 1993-US5436 19930603; JP 06509479 W WO 1993-US5436 19930603, JP 1994-500887 19930603; AU 658073 B AU 1993-44090 19930603; CA 2114719 C CA 1993-2114719 19930603; EP 605674 B1 EP 1993-912364 19930603, WO 1993-US5436 19930603; DE 69316572 E DE 1993-616572 19930603, EP 1993-912364 19930603, WO 1993-US5436 19930603; ES 2114053 T3 EP 1993-912364 19930603; JP 3143694 B2 WO 1993-US5436 19930603, JP 1994-500887 19930603

FDT AU 9344090 A Based on WO 9324840; EP 605674 A1 Based on WO 9324840; JP 06509479 W Based on WO 9324840; AU 658073 B Previous Publ. AU 9344090, Based on WO 9324840; EP 605674 B1 Based on WO 9324840; DE 69316572 E Based

on EP 605674, Based on WO 9324840; ES 2114053 T3 Based on EP 605674; JP 3143694 B2 Previous Publ. JP 06509479, Based on WO 9324840

PRAI US 1992-892865 19920603

REP 5.Jnl.Ref

IC ICM **C12Q001-56**; **G01N033-86**
ICS A01N037-10; **C12Q001-32**; **C12Q001-37**; **G01N033-50**; **G01N033-92**

AB US 5266462 A UPAB: 19960322

Determining the risk of **thrombosis** in a patient by determining the pro-**coagulant** activity of resting **platelets** comprises; (a) mixing a sample containing **platelets** from a patient with a substrate (I) which can be converted by a pro-**coagulant** **phospholipid** dependent enzyme or enzyme complex; (b) contacting and reacting the mixture with the enzyme or enzyme complex to form an **activated** substrate; (c) determining the amount of the formed **activated** substrate in the sample; (d) **comparing** the amount of **activated** substrate with the amount of formed **activated** substrate from one or more control individuals.

Also claimed is a **method** for determining the risk of **thrombosis** in a patient by determining the excitability of platlets by (i) incubating a sample containing **platelets** from a patient with **thrombin** or thormbin plus collagen; (ii) mixing the prod. with (I); (iii) as for step (b) above; (iv) as for step (c) above; and (v) **comparing** the excitability of **platelets** from the patient with the excitability of **platelets** from one or more control individuals. The **method** is also claimed for determining if an agent (II) will effectively inhibit **platelet** **activation**. The sample containing **platelets** is incubated iwth **thrombin** (or **thrombin** plus collagen) and (II), then mixed with (I) and reacted with the enzyme or enzyme complex. The amount of formed **activated** substrate from the sample containing (II) is **compared** with the amount of formed **activated** substrate from a (II)-free sample.

USE/ADVANTAGE - The resting activty and/or excitability of **platelets** can be used to determine patients at risk of **thrombosis** (as claimed). The test is based on the amount of pro-**coagulant** **phospholipids** which are exposed at the outer membrane of **platelets**. The flip-flop reaction of pro-**coagulant** **phospholipids** together with the ability to determine the presence of pro-**coagulant** phospolipids in the outer membrane also provides the basis for the evaluation fo (II) (e.g. drugs) which, e.g. inhibit the flip-flop reaction.

Dwg.0/18

Dwg.0/18

FS CPI EPI

FA AB; DCN

MC CPI: B04-B01B; B04-B02C3; **B04-B04D3**; **B04-B04D5**; B05-B01P; B11-C08E3; **B12-K04A2**; D05-A02C; **D05-H09**
EPI: **S03-E14H1**

ABEQ EP 605674 B UPAB: 19980223

Determining the risk of **thrombosis** in a patient by determining the pro-**coagulant** activity of resting **platelets** comprises; (a) mixing a sample contg. **platelets** from a patient with a substrate (I) which can be converted by a pro-**coagulant** **phospholipid** dependent enzyme or enzyme complex; (b) contacting and reacting the mixt. with the enzyme or enzyme complex to form an **activated** substrate; (c) determining the amt. of the formed **activated** substrate in the sample; (d) **comparing** the amt. of **activated** substrate with the amt. of formed **activated** substrate from one or more control individuals.

Also claimed is a **method** for determining the risk of **thrombosis** in a patient by determining the excitability of platlets by (i) incubating a sample contg. **platelets** from a

patient with **thrombin** or thormbin plus collagen; (ii) mixing the prod. with (I); (iii) as for step (b) above; (iv) as for step (c) above; and (v) **comparing** the excitability of **platelets** from the patient with the excitability of **platelets** from one or more control individuals. The **method** is also claimed for determining if an agent (II) will effectively inhibit **platelet activation.** The sample contg. **platelets** is incubated iwth **thrombin** (or **thrombin** plus collagen) and (II), then mixed with (I) and reacted with the enzyme or enzyme complex. The amt. of formed **activated** substrate from the sample contg. (II) is compared with the amt. of formed **activated** substrate from a (II)-free sample.

USE/ADVANTAGE - The resting activty and/or excitability of **platelets** can be used to determine patients at risk of **thrombosis** (as claimed). The test is based on the amt. of pro-coagulant **phospholipids** which are exposed at the outer membrane of **platelets.** The flip-flop reaction of pro-coagulant **phospholipids** together with the ability to determine the presence of pro-**coagulant** phospolipids in the outer membrane also provides the basis for the evaluation fo (II) (e.g. drugs) which, e.g. inhibit the flip-flop reaction.
Dwg.0/18

L62 ANSWER 35 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **1993-379548** [48] WPIX
DNN **N1993-293156** DNC **C1993-168407**
TI Measuring **protein C** or S activity in **plasma** - by **activation** with **thrombomodulin** and determn. of its effect on endogenous **thrombin** formation, especially for assessing risk of **thrombosis.**
DC B04 D16 J04 S03
IN AIACH, M G H; PITTET, J R
PA (**INMR**) BIO MERIEUX
CYC 1
PI FR 2689640 A1 19931008 (199348)* 21 G01N033-52 <--
ADT FR 2689640 A1 FR 1992-4184 19920406
PRAI FR 1992-4184 19920406
IC ICM **G01N033-52**
AB FR 2689640 A UPAB: 19940120
Determn. of **protein C** and/or S in a **plasma** sample comprises:

a) preparing a mixture of:
(i) **plasma** sample;
(ii) a predetermined quantity of **thrombomodulin**;
(iii) at least one **activated coagulation** factor and/or at least one **coagulation** factor **activator** to allow the formation of endogenous **thrombin**;

b) incubating the obtd. mixture in conditions allowing **activation** of **protein C** and expression of **activated protein C**;

c) adding a **thrombin** substrate to the mixture;

and d) quantifying the **protein C** and/or S activity in the sample by the determn. of enzyme activity of the **thrombin** on the substrate.

Pref. the mixture is incubated for 3-6 (5) minutes at 37 deg. C.

The **thrombomodulin** may be human or animal, natural or recombinant, and/or modified, especially by an enzyme such as chondroitinase, trypsin, elastase or analogues, and is pref. soluble.

The **activated coagulation** factors are pref. **activated** factors XII and/or X. The substrate is pref. fibrinogen.

ADVANTAGE - A simple, easily automated, sensitive process which does not require the use of an exogenous **activator** and can be used even for low concns. of **proteins C** and/or S.

Dwg.
FS CPI EPI
FA AB; GI
MC CPI: B04-B04A6; **B04-B04D3**; **B04-B04D4**; B11-C08E3; **B12-K04A2**; D05-A02C; **D05-H09**; J04-C02
EPI: **S03-E14H1**

L62 ANSWER 36 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1993-321661 [41] WPIX
DNC C1993-143097
TI **Turbidimetric** agglutination assay for use in centrifugal analyser - involves **comparing turbidity** decrease of analyte with known analyte concentration after reaction under centrifugal conditions, useful for e.g. **clotting** proteins.
DC A89 B04 D16 J04
IN KRAUS, M
PA (BEHW) BEHRINGWERKE AG; (DADE-N) DADE BEHRING MARBURG GMBH
CYC 18

PI	DE 4211351	A1	19931007 (199341)*	15	G01N033-50	<--
	EP 568797	A1	19931110 (199345) GE	20	G01N033-546	<--
	R: AT BE CH DE DK ES FR GB IT LI LU NL PT SE					
	AU 9335653	A	19931007 (199346)		G01N021-59	
	CA 2093307	A	19931005 (199401)		G01N033-546	<--
	JP 06018528	A	19940125 (199408)	15	G01N033-543	<--
	AU 661764	B	19950803 (199539)		G01N021-59	
	US 5571728	A	19961105 (199650)	14	G01N033-546	<--
	EP 568797	B1	19991215 (200003) GE		G01N033-546	<--
	R: AT BE CH DE DK ES FR GB IT LI LU NL PT SE					
	DE 59309900	G	20000120 (200011)		G01N033-546	<--
	ES 2141735	T3	20000401 (200023)		G01N033-546	<--
	JP 3327484	B2	20020924 (200264)	15	G01N033-546	<--

ADT DE 4211351 A1 DE 1992-4211351 19920404; EP 568797 A1 EP 1993-104120 19930313; AU 9335653 A AU 1993-35653 19930402; CA 2093307 A CA 1993-2093307 19930402; JP 06018528 A JP 1993-76036 19930402; AU 661764 B AU 1993-35653 19930402; US 5571728 A US 1993-41210 19930401; EP 568797 B1 EP 1993-104120 19930313; DE 59309900 G DE 1993-509900 19930313, EP 1993-104120 19930313; ES 2141735 T3 EP 1993-104120 19930313; JP 3327484 B2 JP 1993-76036 19930402
FDT AU 661764 B Previous Publ. AU 9335653; DE 59309900 G Based on EP 568797; ES 2141735 T3 Based on EP 568797; JP 3327484 B2 Previous Publ. JP 06018528
PRAI DE 1992-4211351 19920404
IC ICM G01N021-59; **G01N033-50**; **G01N033-543**; **G01N033-546**
ICS G01N021-82; **G01N033-53**
ICA **G01N033-531**; **G01N033-86**
AB DE 4211351 A UPAB: 19931130
Determn. of an analyte in a sample is effected by incubating the sample with an analyte-specific binding reagent (immobilised) on a particulate support, where: (a) the reaction takes place under the influence of a centrifugal force which remains constant throughout the measurement process; (b) the particle concentration in the reaction mixture is at least 0.1 weight%; (c) the decrease in **turbidity** is measured (sic measurement is commenced) immediately after the mixing and distribution phase instigated by sample addition; and (d) the analyte concentration is determined by
comparing the **turbidity** decrease for the sample with the values obtained under identical conditions for samples with known analyte contents.
USE/ADVANTAGE - The **method** may be used to determine proteins or peptides of the **clotting**, fibrinolysis or complement system, especially the **fibrin** cleavage prod. D-dimer. The **method** gives quantitative results, with good precision and reproducibility within the **time** (3-8 min.) required for use in

conventional automatic centrifugal analysers.
Dwg.0/0
FS CPI
FA AB
MC CPI: A12-L04; A12-V03C2; B04-B04A; B04-B04C6; B04-C01; B11-C07A6; B12-K04; D05-H09; D05-H13; J04-B01
ABEQ EP 568797 A UPAB: 19931220
Determn. of an analyte in a sample is effected by incubating the sample with an analyte-specific binding reagent (immobilised) on a particulate support, where: (a) the reaction takes place under the influence of a centrifugal force which remains constant throughout the measurement process; (b) the particle concn. in the reaction mixt. is at least 0.1 wt.%; (c) the decrease in **turbidity** is measured (sic measurement is commenced) immediately after the mixing and distribution phase instigated by sample addn.; and (d) the analyte concn. is determined by **comparing** the **turbidity** decrease for the sample with the values obtained under identical conditions for samples with known analyte contents.
USE/ADVANTAGE - The **method** may be used to determine proteins or peptides of the **clotting**, fibrinolysis or complement system, esp. the **fibrin** cleavage prod. D-dimer. The **method** gives quantitative results, with good precision and reproducibility within the **time** (3-8 min.) required for use in conventional automatic centrifugal analysers.
Dwg.0/6
ABEQ US 5571728 A UPAB: 19961211
Determining the concn. of an analyte in <8 mins. comprises:
a) mixing and distributing in an automatic centrifugal analyzer a sample of a biological material contg. the analyte with 1 binding partner specific for the analyte, said binding partner being immobilized on a particulate carrier material wherein the concn. of the particulate carrier material in the mixt. is >0.09 wt.%;
b) maintaining constant centrifugal acceleration of 10-10000 g during the mixing and distributing step;
c) determining a decrease in absorption as a measurement of **turbidity** immediately upon completion of the mixing and distributing step, and
d) determining the concn. of the analyte by **comparing** the measurement of **turbidity** obtained in step c) with values measured under identical conditions for samples of known analyte content.
Dwg.0/6

L62 ANSWER 37 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **1993-182573** [22] WPIX
DNN **N1993-140319** DNC **C1993-080921**
TI **Method** for diagnosing **blood coagulation** disorders e.g. **thromboembolism** - using in-vitro **coagulation** assay including **activated protein C.**
DC B04 D16 S03
IN DAHLBACK, B; DAHLBAECK, B
PA (DAHL-I) DAHLBACK B; (DAHL-I) DAHLBAECK B; (TACT-N) TAC THROMBOSIS & COAGULATION AB
CYC 19
PI WO 9310261 A1 19930527 (199322)* EN 26 C12Q001-56 <--
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE
W: AU CA JP US
SE 9103332 A 19930514 (199329) G01N033-86 <--
AU 9221980 A 19930615 (199340) C12Q001-56 <--
SE 470274 B 19931220 (199402) G01N033-86 <--
EP 608235 A1 19940803 (199430) EN C12Q001-56 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
JP 07501217 W 19950209 (199515) C12Q001-56 <--

	US 5443960	A	19950822 (199539)		7	C12Q001-56	<--
	EP 608235	B1	19960110 (199607)	EN	19	C12Q001-56	<--
	R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE						
	DE 69207607	E	19960222 (199613)			C12Q001-56	<--
	AU 666484	B	19960215 (199614)			C12Q001-56	<--
	ES 2081618	T3	19960316 (199618)			C12Q001-56	<--
	JP 2562000	B2	19961211 (199703)		8	C12Q001-56	<--
	CA 2119761	C	19971216 (199810)			C12Q001-56	<--
	US 5443960	B1	19990112 (199910)			C12Q001-56	<--

ADT WO 9310261 A1 WO 1992-SE310 19920513; SE 9103332 A SE 1991-3332 19911113; AU 9221980 A AU 1992-21980 19920513; SE 470274 B SE 1991-3332 19911113; EP 608235 A1 EP 1992-913443 19920513, WO 1992-SE310 19920513; JP 07501217 W WO 1992-SE310 19920513, JP 1993-509186 19920513; US 5443960 A WO 1992-SE310 19920513, US 1994-199328 19940527; EP 608235 B1 EP 1992-913443 19920513, WO 1992-SE310 19920513; DE 69207607 E DE 1992-607607 19920513, EP 1992-913443 19920513, WO 1992-SE310 19920513; AU 666484 B AU 1992-21980 19920513; ES 2081618 T3 EP 1992-913443 19920513; JP 2562000 B2 WO 1992-SE310 19920513, JP 1993-509186 19920513; CA 2119761 C CA 1992-2119761 19920513; US 5443960 B1 WO 1992-SE310 19920513, US 1994-199328 19940527

FDT AU 9221980 A Based on WO 9310261; EP 608235 A1 Based on WO 9310261; JP 07501217 W Based on WO 9310261; US 5443960 A Based on WO 9310261; EP 608235 B1 Based on WO 9310261; DE 69207607 E Based on EP 608235, Based on WO 9310261; AU 666484 B Previous Publ. AU 9221980, Based on WO 9310261; ES 2081618 T3 Based on EP 608235; JP 2562000 B2 Previous Publ. JP 07501217, Based on WO 9310261; US 5443960 B1 Based on WO 9310261

PRAI SE 1991-3332 19911113; US 1991-811303 19911220

REP 1.Jnl.Ref; EP 434377; SE 464135; WO 9101282; WO 9102812; 6.Jnl.Ref

IC ICM **C12Q001-56**; **G01N033-86**
ICS **G01N033-50**

AB WO 9310261 A UPAB: 19931115

An in vitro **method** for the diagnosis of **blood coagulation** disorders, in partic. **thromboembolic** diseases in a human or for the detection of the risk for a human to acquire **blood coagulation** disorders, where the disorders are not expressed by Protein S deficiency or defective Factor VIIIa, or the disorders are not related to Protein S deficiency, comprising (i) incubating a sample containing human **coagulation** factors with (a) an exogenous reagent (I) which at least partially **activates** the **blood coagulation** system of the sample, (b) an **activated** exogenous **Protein C** (APC) or exogenous PC together with exogenous reagents (II) that transform exogenous PC to APC, components, such as **phospholipid** and Ca(2+) salt, are necessary for efficient reaction of the **activated coagulation** factors introduced in step (1, a) and (d) if desired, an exogenous sustrate for an eznyme, which activity is influenced by **activated Protein C**, the final assay media pref. having at least a patient **plasma** sample content that is greater than 10%, in partic. greater than 20% or 35% (v/v), (ii) directly monitoring a substrate conversion **rate** for a **blood coagulation** eznyme which activity is influenced by **activated Protein C** and (iii) **comparing** the conversion **rate** determined in step (ii) with a **standard** value obtd. from samples of **normal** individuals subjected to steps (i) and (ii) under identical conditions; where the finding of a sample conversion **rate** that is not **normal compared** to the **standard** value is taken as an indication of the human suffering from the disorder or as being at risk for acquiring the disorder, in partic. an enhanced conversion **rate** is taken as an indication of a **thromboembolic** disease or a risk for acquiring such disease.

Reagent (I) may be e.g. Factor Ax, Factor IXa or an APTT reagent.

USE/ADVANTAGE - The **method** can be used for screening and diagnosis of e.g. hereditary **thrombophilia**, in pregnant

individuals, individuals undergoing surgery, individuals taking anti-conception drugs, etc.
Dwg. 0/0
FS CPI EPI
FA AB
MC CPI: B04-B01B; B04-B02C3; B04-B04A6; **B04-B04D3**; **B04-B04D4**; B05-A01B; B05-B01P; B11-C08E; **B12-K04A2**; **D05-H09**
EPI: **S03-E14H1**
ABEQ US 5443960 A UPAB: 19951004
In vitro screening and diagnosis of **activated protein C**(APC) resistance comprises (i) incubating human **plasma** with (a) exogenous APC, **protein C** and an exogenous reagent (b) an exogenous reagent partially **activating** a **coagulation** factor and opt. (c) an exogenone substrate for an enzyme affected by APC; (ii) measuring substrate conversion **rate** for a **coagulation** factor affected by APC; and (iii) **comparing** this with a **std.** value. Higher than **std.** values indicate APC resistance. Resistance is recognised by a low anti-**coagulant** response to exogenous APC not related to protein S deficiency or defective factor VIII/VIIIa, and has a low anti-**coagulant** response to exogenous APG in the absence of APC Ig inhibitors.
USE - Used for detecting APC resistance e.g. in screening and diagnosing **thromboembolic** diseases such as hereditary **thrombopilia.** Also for determining the risk of **thrombosis** in pregnancy, surgery and during contraceptive use.
Dwg.0/0
ABEQ EP 608235 B UPAB: 19960222
An in vitro **method** for diagnosing in a human, or for determining the risk for a human to acquire manifestation of, **blood coagulation** disorder designated APC resistance and recognized by an abnormally low **anticoagulant** response to exogenous **activated Protein C** (abbreviated APC) even in presence of **normal** levels of functional Protein S, a Factor VIIIa, which is **normally** degraded by APC, and absence of lupus **anticoagulants**, said **method** comprising determining for a **plasma** sample comprising **coagulation** factors and derived from a human, the **anticoagulant** activity of exogenous APC by measuring the substrate conversion **rate** obtained for a **blood coagulation** enzyme, the activity of which is influenced by APC, by the following steps: (i) incubating said **plasma** sample with (1) exogenous APC, or exogenous **Protein C** together with current exogenous reagents to transform the exogenous **Protein C** to APC; (2) an exogenous Reagent (I), which at least partially **activates** the **blood coagulation** system of said sample and is selected in a manner known per se to cause **activation** of a **coagulation** factor used for the measurement in step (ii); (3) components such as **phospholipid**(s) and Ca** salt, that are necessary to efficient reaction of the **activated coagulation** factors introduced by step (i)(2); and if desired, (4) an exogenous substrate for an enzyme, the activity of said enzyme being influenced by APC; (ii) directly measuring said substrate conversion **rate** obtained in (i), and (iii) **comparing** the conversion **rate** measured in step (ii) with a **standard** value obtained from samples from **normal** individuals, which samples have been subjected to steps (i) and (ii) under essentially the same conditions as the **plasma** sample from said human; in which **method** a substrate conversion **rate** obtained for a **plasma** sample in step (ii), that is higher than the **standard** value indicates that said human suffers from or runs the risk of acquiring manifestation of said disorder.
Dwg.0/0

L62 ANSWER 38 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1992-066428 [09] WPIX
DNN N1992-049884 DNC C1992-030418
TI Immunoassays using soluble **fibrin** monomer - comprising **fibrin**-like material, avoiding solubility maintaining reagent or **polymerisation** inhibitor, for plasmin **activator** determn..
DC B04 S03
IN KUDRYK, B J; PROCYK, R
PA (NYBL-N) NEW YORK BLOOD CENTER INC; (NYBL-N) NEW YORK BLOOD CEN; (PROC-I) PROCYK R; (NYBL-N) NY BLOOD CENT INC; (NYBL-N) NEW YORK BLOOD CENT INC
CYC 19
PI EP 472205 A 19920226 (199209)*
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
AU 9182628 A 19920227 (199218)
CA 2049710 A 19920224 (199220) G01N033-573 <--
JP 04233458 A 19920821 (199242) 13 G01N033-53 <--
AU 644205 B 19931202 (199404) G01N033-68 <--
EP 472205 B1 19970108 (199707) EN 18 G01N033-86 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
DE 69124030 E 19970220 (199713) G01N033-86 <--
US 6074837 A 20000613 (200035) C12Q001-56 <--
KR 171609 B1 19990501 (200051) G01N033-50 <--
ADT EP 472205 A EP 1991-114134 19910823; CA 2049710 A CA 1991-2049710 19910822; JP 04233458 A JP 1991-208131 19910820; AU 644205 B AU 1991-82628 19910820; EP 472205 B1 EP 1991-114134 19910823; DE 69124030 E DE 1991-624030 19910823, EP 1991-114134 19910823; US 6074837 A Cont of US 1990-572189 19900823, Cont of US 1992-946826 19920917, Cont of US 1994-308482 19940919, US 1995-468460 19950606; KR 171609 B1 KR 1991-14643 19910823
FDT AU 644205 B Previous Publ. AU 9182628; DE 69124030 E Based on EP 472205
PRAI US 1990-572189 19900823; US 1992-946826 19920917;
US 1994-308482 19940919; US 1995-468460 19950606
REP 2.Jnl.Ref; EP 94720; WO 8605814; WO 8900005
IC ICM **C12Q001-56**; **G01N033-50**; **G01N033-53**; **G01N033-573**; **G01N033-68**; **G01N033-86**
ICS C12P021-02; C12P021-06; **C12Q001-37**; G01N003-68
AB EP 472205 A UPAB: 19931006
Reagent is a fibrinolytic material having a solubility and stability similar to fibrinogen in that it remains soluble and stable at physiological conditions at a concentration used in the assay in the absence of **fibrin polymerisation** inhibitors or reagents for maintaining solubility.
USE/ADVANTAGE - Quantitative determn. of soluble **fibrin** monomers, plasmin **activator** inhibitor activity, tissue-plasminogen **activator** in **plasma** and immunoassays. Difficulty of solubilising **fibrin** under physiological conditions, useful for form of **fibrin**, or a substance with the properties of **fibrin**, that does not require special conditions for maintaining solubility especially in biochemical and immunological assays that require **fibrin** monomer or soluble **fibrin**.
1/6
FS CPI EPI
FA AB; GI
MC CPI: B04-B02C3; **B04-B04D**; B11-C07A; B11-C08; B12-K04A
EPI: S03-**E14H1**
ABEQ EP 472205 B UPAB: 19970212
An assay **method** that requires a soluble **fibrin** or a soluble **fibrin** monomer reagent as one of the components of the assay, wherein the reagent is a **fibrin**-like material having a solubility and stability similar to fibrinogen in that it remains soluble

and stable at physiological conditions at a concentration employed in the assay and substantially identical to that produced by a process comprising the following steps: (1) partially reducing fibrinogen with a low amount of reducing agent, at slightly elevated temperature, under non-denaturing conditions, in the absence of divalent **cations**, and for a **time** sufficient to allow almost complete cleavage of susceptible disulphide bonds of the fibrinogen to free thiol groups, then (2) blocking said thiol groups with a blocking reagent, then optionally (3) reacting the product of step (2) with a **clotting** enzyme in physiological buffers in the absence of divalent **cations** to release fibrinopeptides A and B, and thereafter (4) terminating the activity of said **clotting** enzyme.
Dwg.0/6

L62 ANSWER 39 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **1991-193318** [26] WPIX
DNN **N1991-147980** DNC **C1991-083712**
TI Improved fibrinogen assay avoids repeated calibration curves - avoids repeated calibration curves since single calibration only is required to convert sensor signal to concentration.
DC B04 J04 S03 S05
IN CALLAHAN, J B; HOFFMAN, J F; SWOPE, C H; CALLAHAN, J
PA (**ALKU**) AKZO NV; (**ALKU**) **AKZO NOBEL NV**
CYC 21
PI WO 9108460 A 19910613 (199126)*
RW: AT BE CH DE DK ES FR GB GR IT LU NL SE
W: AU CA FI JP KR US
AU 9168983 A 19910626 (199139)
FI 9202312 A 19920521 (199235) G01N
EP 502103 A1 19920909 (199237) EN G01N021-00
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
ZA 9009564 A 19921125 (199301) 13 G01N000-00
JP 05503008 W 19930527 (199326) 5 C12Q001-56 <--
US 5223437 A 19930629 (199327) 3 G01N021-00
AU 641459 B 19930923 (199345) C12Q001-56 <--
EP 502103 A4 19930505 (199526)
ADT FI 9202312 A WO 1990-US6988 19901130, FI 1992-2312 19920521; EP 502103 A1 WO 1990-US6988 19901130, EP 1991-900512 19901130; ZA 9009564 A ZA 1990-9564 19901128; JP 05503008 W WO 1990-US6988 19901130, JP 1991-501113 19901130; US 5223437 A Cont of US 1989-443948 19891201, US 1991-696569 19910508; AU 641459 B AU 1991-68983 19901130; EP 502103 A4 EP 1991-900512
FDT EP 502103 A1 Based on WO 9108460; JP 05503008 W Based on WO 9108460; AU 641459 B Previous Publ. AU 9168983, Based on WO 9108460
PRAI US 1989-443948 19891201
REP 1.Jnl.Ref; US 3658480; US 3833864; US 3861877; US 3989382; US 4659550; US 4720787; EP 184242; EP 59277; US 3432268; US 3905769
IC ICM **C12Q001-56**; G01N000-00
ICS G01N021-59; G01N021-75; G01N021-77; **G01N033-86**
AB WO 9108460 A UPAB: 19950301
A **method** for optically measuring the concentration of fibrinogen in a **blood plasma** sample comprises: (a) providing a sample of **plasma** containing fibrinogen in a container; (b) adding **thrombin** to the sample, and mixing; (c) measuring the initial optical transmittance Ti for the reaction mixture; (d) allowing the **thrombin** and fibrinogen in the mixture to react; (e) measuring a final optical transmittance Tf for the reaction mixture; (f) **comparing** Tf with Ti to compute a delta value; and (g) determining the concentration of fibrinogen based on the delta value.
USE/ADVANTAGE - Prior art **methods** of determining fibrinogen concentration by **clotting methods** depend on repeated construction of calibration curves, involve considerable calculation and are time consuming. Also the quantity being measured is often instrument and **time** dependent. The present **method**

eliminates the need to establish a **standard** curve repeatedly, as it need be done only once. This is constructed so that it remains unchanged by variations, instrument, or sample. Once the correlation equation for R is established, it can be permanently stored in the computer software. @(12pp Dwg.No.0/0)
0/0

FS CPI EPI
FA AB
MC CPI: **B04-B04D2**; **B04-B04D4**; B11-C07B2; B11-C09; B12-K04A; J04-B01B
EPI: S03-E04B1; **S03-E14H1**; S05-C01

ABEQ JP 05503008 W UPAB: 19931116
A method for optically measuring the concn. of fibrinogen in a **blood plasma** sample comprises: (a) providing a sample of **plasma** contg. fibrinogen in a container; (b) adding **thrombin** to the sample, and mixing; (c) measuring the initial optical transmittance Ti for the reaction mixt.; (d) allowing the **thrombin** and fibrinogen in the mixt. to react; (e) measuring a final optical transmittance Tf for the reaction mixt.; (f) **comparing** Tf with Ti to compute a delta value; and (g) detg. the concn. of fibrinogen based on the delta value.
USE/ADVANTAGE - The **method** eliminates the need to establish a **standard** curve repeatedly, as it need be done only once. This is constructed so that it remains unchanged by variations, instrument, or sample, Once the correlation equation for R is established, it can be permanently stored in the computer software.

ABEQ US 5223437 A UPAB: 19931116
Optically measuring a concn. of fibrinogen in a **blood plasma** sample comprises adding **thrombin** to a sample of **plasma** contg. fibrinogen in a container, mixing the **thrombin** with the sample, measuring an initial optical transmittance for the obtd. reaction mixt., allowing the **thrombin** and fibrinogen to react, measuring a final optical transmittance for the reaction mixt., **comparing** the final transmittance measurement to the initial transmittance measurement to compute a delta value and determining the concn. of fibrinogen based on the delta value.
Pref., the **thrombin** is at a concn. of 100 N1H units and the **plasma** sample is diluted in a 1:10 **ratio** with Na barbital.
ADVANTAGE - **Method** has improved efficiency. The effects of instrument and channel variation in measuring the changes in optical transmission, are eliminated.
Dwg.0/3

L62 ANSWER 40 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1986-108161 [17] WPIX
DNN N1986-079665 DNC C1986-046181
TI Monitoring **coagulation** of fibrinogen - avoiding early false positives due to noise.
DC B04 J04 S03
IN LIPSCOMB, M S
PA (INNO-N) INNOVATIVE MEDICAL SYSTEMS; (ORTH) ORTHO DIAGNOSTIC SYSTEMS INC
CYC 16
PI EP 178910 A 19860423 (198617)* EN 26
R: AT BE CH DE FR GB IT LI LU NL SE
AU 8548728 A 19860424 (198624)
JP 61128172 A 19860616 (198630)
ES 8704637 A 19870616 (198729)
US 4720787 A 19880119 (198805)
CA 1236921 A 19880517 (198824)
EP 178910 B 19920108 (199203)
R: AT BE CH DE FR GB IT LI LU NL SE
DE 3585129 G 19920220 (199209)

JP 06230011 A 19940819 (199438) 11 G01N033-86 <--
JP 07082020 B2 19950906 (199540) 9 G01N033-86 <--
JP 2500848 B2 19960529 (199626) 12 G01N033-86 <--

ADT JP 61128172 A JP 1985-229787 19851015; ES 8704637 A ES 1985-547898 19851015; US 4720787 A US 1985-786925 19851011; JP 06230011 A Div ex JP 1985-229787 19851015, JP 1993-342245 19851015; JP 07082020 B2 JP 1985-229787 19851015; JP 2500848 B2 Div ex JP 1985-229787 19851015, JP 1993-342245 19851015

FDT JP 07082020 B2 Based on JP 61128172; JP 2500848 B2 Previous Publ. JP 06230011

PRAI GB 1984-26004 19841015

REP 5.Jnl.Ref; A3...8627; A3...8846; DE 2635081; DE 3230672; DE 3439344; EP 107498; EP 109234; EP 117470; EP 128009; EP 131789; EP 77063; EP 80032; EP 87686; EP 88540; FR 2408839; GB 2040292; No-SR.Pub; US 4279616; WO 8301198

IC **C12Q001-56**; **G01N033-49**
ICM G01N033-86
ICS C12Q001-56; **G01N033-49**

AB EP 178910 A UPAB: 19970502
The presence of a **coagulation** component (I) in a mixture of **coagulation** reagent and patient sample uses a sensor for determining increases in optical density and provides a coordinating signal. (a) The value of the signal proportional to the optical property of the mixture at various **times** during a predetermined interval after formation of the mixture is measured and stored; (b) the value of the signal at the end of the predetermined interval is determined; (c) the stored signal values are scanned starting with the last acquired signal to determine the **time** T1 when the measured signal is less than or equal to X **times** the determined end value; (d) the stored signal values are scanned starting with the last acquired signal to determine the **time** T2 when the measured signal is less than or equal to Y **times** the determined end value when X is greater than and less than 1; (e) a function relating the measured signal to **time** is produced by performing a curve fitting analysis of the measured signal values over a **time** period bounded by T1 and T2; and (f) the **time** at which the value of the signal is equal to Z **times** the determined end value is determined from the function where Z = 0-1 exclusive whereby the (I) **clotting** detection **time** is determined.S ADVANTAGE - **Method** shows high sensitivity for detection of **clotting times** due to reduction of noise effects in the **clotting time.** It provides statistically valid data which may be used to set confidence levels on the final **clotting time** results, especially valuable in that it permits singlet sample testing as opposed to prior art required double sample testing. This reduces by half the amount of reagents and personnel required and increases throughput capacity.
Dwg.0/0

FS CPI EPI

FA AB

MC CPI: B04-**B04D2**; B11-C08; **B12-H04**; B12-K04A; J04-B01; J04-C04
EPI: S03-**E14H1**

ABEQ EP 178910 B UPAB: 19930922
Method for measuring blood clotting time by monitoring the prsence of a **coagulation** component in a mixture of **coagulation** reagent and patient sample and employing a sensor for determining increases in optical density and providing a signal proportional thereto, comprising: a) measuring and storing the value of the signal proportional to the optical property of the mixture at a plurality of **times** during a predetermined interval after formation of the mixture; b) determining the value (Vmax) of the signal at the end of the predetermined interval; c) scanning the stored signal values starting with the last acquired signal to determine the time T1 when the measured signal is less than or equal to X

times the determined end value (Vmax); d) scanning the stored signal values starting with the last acquired signal to determine the **time** T2 when the measured signal is less than or equal to Y **times** the determined end value wherein 1 is above 1 which is above Y which is above X which is above O, and X and Y are determined experimentally; e) statistically calculating a function relating the measured signal to **time** by performing a curved fitting analysis of the measured signal values over a **time** period bounded by **times** T1 and T2; and f) determining the **blood clotting time** from said function, said **blood clotting time** being the **time** at which the value of the signal is equal to Z **times** the statistically determined end value wherein Z is between 1 and 0 and Z is determined empirically.

ABEQ US 4720787 A UPAB: 19930922

System for monitoring presence of a **coagulation** component in a mixt. of **coagulation** reagent and patient sample involves measuring component **clotting** detection **time** and employing a sensor to determine increase in optical density and providing a signal in coordination.

Values of the signal proportional to the optical property of the mixt. are measured and stored during a predetermined interval after mixt. formation. The last stored value of the signal is determined at the end of the predetermined interval, all stored signal values are scanned starting with the last stored signal value to determine a **time** T1 when the measured signal exceeds or equals a fraction X **times** the last stored signal value. The stored signal values starting with the last value are further scanned starting with the last stored signal value to determine a **time** T2 when the measured signal is less than or equal to a fraction Y **times** the last stored signal, where Y is less than 1 and X is less than Y. A function relating stored signal values to **times** is produced by curve fitting analysis of the stored signal for **times** between T1 and T2. From this function, the time at which the value of the signal equals Z **times** the last stored signal value is determined, where Z is 0-1 (exclusive). Hence component **clotting** detection **time** is determined.

USE - For fibrinogen determn. and in **thrombin**, partial **thromboplastin** and **prothrombin coagulation** tests.

L62 ANSWER 41 OF 41 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **1985-237368** [39] WPIX
DNN **N1985-177516** DNC **C1985-102812**
TI Test composition for partial **thromboplastin time** determination - contains a **platelet** factor reagent and a hydrocarbyl sulphonic or sulphuric acid or salt.
DC B04 B05 S03
PA (**ALKU**) AKZO NV; (WARN) GOEDECKE AG; (WITT-I) WITT P
CYC 13
PI DE 3407280 A 19850919 (198539)* 16
EP 155565 A 19850925 (198539) GE
R: AT BE CH DE FR GB IT LI LU NL SE
JP 60203200 A 19851014 (198547)
US 4672030 A 19870609 (198725)
EP 155565 B 19900425 (199017)
R: AT BE CH DE FR GB IT LI LU NL SE
DE 3577349 G 19900531 (199023)
JP 06004040 B2 19940119 (199406) C12Q001-56 <--
ADT DE 3407280 A DE 1984-3407280 19840228; EP 155565 A EP 1985-102281 19850228; JP 60203200 A JP 1985-38636 19850227; US 4672030 A US 1985-702284 19850215; JP 06004040 B2 JP 1985-38636 19850227
FDT JP 06004040 B2 Based on JP 60203200
PRAI DE 1984-3407280 19840228

REP A3...8647; EP 107383; EP 49877; No-SR.Pub
IC **C12Q001-56**; G01B033-86; **G01N033-86**
ICM **C12Q001-56**
ICS G01B033-86; **G01N033-86**
AB DE 3407280 A UPAB: 19970909
A test composition for partial **thromboplastin time** (PTT) determination with a **platelet** factor reagent also contains at least one cpd. of formula (Ia) (R-O-SO3-X) or (Ib) (R-SO3-X) (where R is opt. substd. singly or multiply unsatd. branched or straight chain aliphatic or cycloaliphatic hydrocarbyl or an opt. substd. aromatic gp; X is H or a **cation**).
USE/ADVANTAGE - The test composition can be used to carry out screening tests for endogenous **coagulation** systems, and in the monitoring of heparin therapy. The reconstituted reagent is stable at 37 deg.C, room temperature and on storage in a fridge The reagent is more sensitive towards heporin than previous reagents.
Dwg.0/0
FS CPI EPI
FA AB
MC CPI: B10-A09A; B10-A09B; B12-K04
EPI: **S03-E14H9**
ABEQ EP 155565 B UPAB: 19930925
Test kit for the PTT determination with a **platelet** factor reagent, characterised in that it additionally contains at least one compound of the formulae R-O-SO3X or R-SO3X in which R stands for an optionally substituted mono- or polyunsaturated, straight-chain or branched aliphatic or cycloaliphatic hydrocarbon radical or an optionally substituted aromatic radical, and X represents a hydrogen atom or a **cation**, is additionally added to the reagent in an amount such that 1l of the reconstituted solution contains 0.05 to 100 mmol thereof.
ABEQ US 4672030 A UPAB: 19930925
Test kit for determn. of partial **thromboplastin time** (PTT) contg. test reagents comprises a PTT reagent and a cpd. (I) of formula R-O-SO3X or R-SO3X (where R is mono- or poly-unsatd. opt. branched (cyclo)aliphatic hydrocarbon gp. or aromatic gp. and is opt. substd.; and X is H or a **cation**).
Pref. 1 l. reconstituted test reagent soln. contains 0.05-100 (0.2-20) mmol. (I). (I) may be dodecylbenzene sulphonic acid-Na salt or Na lauryl sulphate.
USE/ADVANTAGE - In diagnostic tests for the endogenous **coagulation** system. The test kit offers improved sensitivity esp. to low mol. heparin fractions, and enables control of heparin therapy.

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(FILE 'HOME' ENTERED AT 09:30:52 ON 07 JUL 2004)
SET COST OFF

FILE 'WPIX' ENTERED AT 09:31:08 ON 07 JUL 2004
L1 1 S (US20040053351 OR US6743596)/PN OR (WO2001-US32564 OR US2003-
E BIOMER/PA
L2 178 S E6-E17
E INMR/PACO
L3 641 S E3,E4
E AKZO NOBEL/PA
L4 2016 S E3-E29
E ALKU/PACO
L5 4288 S E3-E5
E FISCHER T/AU
L6 176 S E3,E10
E BAGLIN T/AU

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L7            5 S E3,E4
                E TEJIDOR L/AU
L8            8 S E3,E4
                E G01N033-86/IC,ICM,ICS
L9          857 S E3-E7
                E G01N033-86/ICA,ICI
L10          23 S E3,E4
L11           1 S E38
L12         877 S L9-L11
L13          23 S L2-L8 AND L12
L14         151 S L2-L8 AND (S03-E14H1 OR B14-F08 OR C14-F08 OR B12-H04 OR C12-
L15         151 S L2-L8 AND (B04-B04D? OR C04-B04D?)/MC
                E G01N033-49/IC,ICM,ICS
L16        2694 S E3-E5
                E G01N033-49/ICA,ICI
L17          94 S E3,E4
L18           1 S E101
L19        2775 S L16-L18
                E G01N033-50/IC,ICM,ICS
L20       14057 S E3-E5
                E G01N033-50/ICA,ICI
L21         328 S E3,E4
L22           8 S E98
L23       14354 S L20-L22
                E C12Q001-56/IC,ICM,ICS
L24         608 S E3-E7
                E C12Q001-56/ICA,ICI
L25          30 S E3
L26         632 S L24,L25
L27          69 S L2-L8 AND L19,L23,L26
L28         198 S L15,L27
L29           6 S L28 AND FIBRIN/BIX
L30          23 S L28 AND ACTIVAT?/BIX
L31           8 S L28 AND THROMBIN/BIX
L32           4 S L28 AND PROTEIN C/BIX
L33           3 S L28 AND THROMBOMODULIN/BIX
L34           4 S L28 AND TISSUE FACTOR/BIX
L35          40 S L1,L13,L29-L34
L36         163 S L28 NOT L35
L37         176 S L2-L8 AND (P813 OR P815 OR R611)/M0,M1,M2,M3,M4,M5,M6
L38          96 S L37  NOT L28,L36
                SEL DN AN L35 5 6 8 11 13-15 17 25 27 36 40
L39          12 S E1-E35
L40          12 S L1,L39 AND L1-L39
L41         185 S L12 AND L19,L23
L42         325 S L12 AND L26
L43          77 S L41 AND L42
L44          28 S L41 AND FIBRIN/BIX
L45          37 S L41 AND THROMBIN/BIX
L46          12 S L41 AND PROTEIN C/BIX
L47           4 S L41 AND TISSUE FACTOR/BIX
L48         107 S L41 AND TIME/BIX
L49          39 S L48 AND L44-L47
                SEL DN AN L49 2 8-10 13 17 25-27 29 31-33 35-38
L50          22 S L49 NOT E36-E84
L51          31 S L40,L50
L52          53 S L43-L47 NOT L49-L51,L2-L8
                SEL DN AN L52 4 7 21 23 24 27 28 31 41 44
L53          10 S E85-E114
L54          41 S L51,L53 AND L1-L53
L55          41 S L54 AND (?COAGUL? OR ?CLOT? OR ACTIVAT? OR INITIAT? OR THROMB
L56          41 S L54 AND (METHOD? OR  PLASMA OR BLOOD OR SERUM OR CATION? OR H
L57          41 S L54-L56 AND (A61B OR C12Q OR G01N033)/IC,ICM,ICS,ICA,ICI
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L58          41 S L57 AND (B04-H19 OR C04-H19 OR B04-B04D? OR C04-B04D? OR B04-
L59          41 S L54-L58,L1
L60          35 S L59 AND ?THROMB?/BIX
L61           8 S L59 AND (HEME? OR HAEM?)/BIX
L62          41 S L59-L61

     FILE 'WPIX' ENTERED AT 10:40:01 ON 07 JUL 2004

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